HOUSE OF COMMONS

First Session—Twenty-fifth Parliament

1962-1963

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. R. M. T. McDONALD

PROCEEDINGS

No. 1 - 4

WEDNESDAY, DECEMBER 19, 1962

THURSDAY, JANUARY 24, 1963

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1963

28301-0—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. R. M. T. McDonald

Vice-Chairman: Mr. Georges Valade

and Messrs.

Baldwin	Harley	Mitchell
Enns	Horner (*Jasper-Edson*)	Nicholson
Fairweather	Marcoux	Orlikow
Haidasz	Martin (*Essex East*)	Patterson
		Rynard—15

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

ORDERS OF REFERENCE

FRIDAY, December 7, 1962.

Resolved,—That a Special Committee be appointed to consider and report upon (a) the law and practices relating to the control of the introduction, marketing and use of drugs; and (b) the dangers arising from contamination of food by the use of chemicals to kill weeds, insects and other pests;

That the Committee consist of 15 Members to be designated by the House;

That the Committee be empowered to send for persons and papers and to report from time to time;

That the Committee be empowered to sit during the sittings of the House;

That the Committee have power to print such papers and evidence from day to day as may be deemed advisable; and

That Standing Order 66 be suspended in relation thereto.

MONDAY, December 17, 1962.

Ordered,—That the Special Committee on Food and Drugs, appointed on December 7, 1962, be composed of Messrs. Baldwin, Enns, Fairweather, Haidasz, Harley, Horner (*Jasper-Edson*), Marcoux, Martin (*Essex East*), McDonald (*Hamilton South*), Mitchell, Nicholson, Orlikow, Patterson, Rynard, and Valade.

Attest.

LEON-J. RAYMOND,
Clerk of the House.

28301-0—1½

MINUTES OF PROCEEDINGS

WEDNESDAY, December 19, 1962.

(1)

The Special Committee on Food and Drugs met today at 2 p.m. for organization purposes.

Members present: Messrs. Baldwin, Enns, Fairweather, Haidasz, Harley, Martin (*Essex East*), McDonald (*Hamilton South*), Nicholson, Orlikow, Rynard, and Valade—11.

The Clerk of the Committee attending and having called for nominations, it was moved by Mr. Rynard, seconded by Mr. Fairweather, that Mr. McDonald be elected Chairman of the Committee.

Mr. Valade moved, seconded by Mr. Haidasz, that Mr. Rynard be elected Chairman.

And a discussion arising, Mr. Martin opposed the withdrawal of Mr. Valade's motion and requested a recorded vote. The Clerk, being bound by the Rules for the election of the Speaker, stated that she proposed to put the first motion first.

Whereupon Mr. Baldwin expressed the view, in which the Committee concurred, that Dr. Rynard's contribution would be more valuable as a member than as Chairman of the Committee.

By consent, Mr. Valade withdrew his motion.

The first motion being put, Mr. McDonald was unanimously elected Chairman of the Committee.

Mr. McDonald took the Chair and thanked the Committee for the honour conferred upon him.

On motion of Mr. Enns, seconded by Mr. Fairweather,

Resolved,—That Mr. Valade be elected Vice-Chairman of the Committee.

The Chairman then referred to the part of the Order of Reference giving the Committee the powers to sit during the sittings of the House, and to print such papers and evidence from day to day as may be deemed advisable.

On motion of Mr. Martin, seconded by Mr. Baldwin,

Resolved,—That a Subcommittee on Agenda and Procedure comprised of the Chairman and the Vice-Chairman and one representative from each of the Opposition parties be appointed.

After discussion, it was agreed that the Committee set the number of proceedings to be printed at a subsequent meeting.

At 2.25 p.m., on motion of Mr. Nicholson, the Committee adjourned to the call of the Chair.

THURSDAY, January 24, 1963.
(2)

The Special Committee on Food and Drugs met at 9.30 a.m. this day. The Chairman, Mr. R. M. T. McDonald, presided.

Members present: Messrs. Baldwin, Fairweather, Haidasz, Harley, Horner (*Jasper-Edson*), McDonald (*Hamilton South*), Mitchell, Nicholson, Patterson, Rynard, and Valade—11.

The Chairman observed the presence of a quorum. The Clerk of the Committee read the Orders of Reference.

The Chairman announced that, in accordance with the resolution adopted at the first meeting, the following members had been chosen to act with him and the Vice-Chairman on the Subcommittee on Agenda and Procedure, namely: Dr. Haidasz, Mr. Orlikow, and Dr. Marcoux.

At a meeting of the Subcommittee the Chairman stated, it was decided that the Chairman should make a general statement with regard to the terms of reference and then proceed to consider the Agenda that was prepared for the Committee.

Accordingly, the Chairman read his statement into the record including the list of proposed witnesses as well as a schedule of meetings which the Committee approved tentatively.

It was agreed that notice be sent to all the suggested witnesses expressing the desire of the Committee to call them at a later date.

After discussion, it was further agreed that the name of the Minister of Forestry and his officials be added to the list and that the Chairman contact the Department of Justice with a view to having a statement regarding the jurisdiction of the Committee.

On motion of Mr. Valade, seconded by Mr. Horner,

Resolved,—That 750 copies in English and 750 copies in French of the Minutes of Proceedings and Evidence be printed.

Agreed,—That the Committee seek permission of the House to sit in Montreal on Thursday, Friday and Saturday morning, February 14, 15 and 16 next.

At 11 o'clock, on motion of Mr. Baldwin, seconded by Mr. Mitchell, the Committee adjourned until Tuesday, January 29, at 9.30 a.m.

Gabrielle Savard,
Clerk of the Committee.

PROCEEDINGS

THURSDAY, January 24, 1963.

The CHAIRMAN: We have a quorum. First of all, I would like again to thank the members of the committee for electing me chairman of this committee.

We will commence by having the clerk of the committee read the complete terms of reference so that we all know where we stand.

The CLERK OF THE COMMITTEE:

FRIDAY, December 7, 1962.

Resolved that a special committee be appointed to consider and report upon (*a*) the law and practices relating to the control of the introduction, marketing and use of drugs; and (*b*) the dangers arising from contamination of food by the use of chemicals to kill weeds, insects and other pests.

That the committee consist of 15 members to be designated by the house;

That the committee be empowered to send for persons and papers and to report from time to time;

That the committee be empowered to sit during the sittings of the house;

That the committee have power to print such papers and evidence from day to day as may be deemed advisable; and

That standing order 66 be suspended in relation thereto.

The CHAIRMAN: Thank you. The subcommittee on agenda and procedures, comprised of your chairman, vice-chairman, Mr. Valade, Dr. Haidasz, Mr. Orlikow and Dr. Marcoux, met on Tuesday of this week at 11.45 a.m. to discuss the over-all agenda that was prepared by your chairman, and we had a general discussion on the terms of reference. At that time it was decided that the chairman should make a statement with regard to the terms of reference and then proceed to go through the agenda that was prepared for your consideration.

I have several copies of remarks, if some members would like to have a copy. Following this, we then can have a general discussion if the members of the committee deem it to be in order.

The first statement I should like to make concerns the chairman's views related to the terms of reference. I think it probably should be looked at in three ways: safety of drugs, safety of pesticides and the possibility of investigation of prices.

As indicated in the terms of reference, I think the main purpose of this committee is to check into the responsibility of all people in the drug business in Canada in regard to the safety of drugs and into the introduction and handling of drugs and pesticides as well as the marketing of these drugs for public use.

I might say that the report of the special committee of the Royal College of Physicians and Surgeons on drugs will be introduced into the house today and this will enable the members of this committee to become well informed of this special committee's report. I am sure it will assist you in our future discussions.

As far as the price situation is concerned, I, as your chairman, want to be fair about this. I think the Minister of National Health and Welfare has given us certain powers. On December 17, 1962 at page 2242 of *Hansard,* he stated:

Mr. Speaker, in closing this debate I should like to point out that I think it is probably up to the committee itself to determine the definition of the word "marketing" in the resolution.

If we do this in an orderly way—and I hope in a non-political way—we might be of service to the people of this country.

I have had passed out copies of the agenda and, with your permission, I would like to start with the drug situation in connection with safety aspects and then go on to the pesticides and contamination of food, followed by the price discussion at the end. In this way we will be able to proceed in an orderly way.

The first section is the drug safety section which, I think, should be broken down into subsections, as discussed by the subcommittee. The first section would deal with the law and practices relating to the control of the introduction, marketing and use of drugs in Canada and this, no doubt should be broken down into a number of sections:

1. (*a*) The control of the introduction, marketing and use of drugs under the Food and Drugs Act and the regulations; (*b*) preclinical testing of drugs with reference to an evaluation of the safety of new drugs by means of tests on animals; (*c*) existing practices in respect of the testing of drugs in humans for the purpose of assessing safety and effectiveness; (*d*) a general appraisal of the present day practices in respect of the preclinical and clinical testing of drugs for marketing, and (*e*) existing practices in respect of the marketing of drugs.

2. Report by the chairman of the special committee of the Royal College of Physicians and Surgeons, under the direction of Dr. Brien. As indicated before, this report will be tabled in the house today by the Minister of National Health and Welfare and,

3. Report on existing legislation in various countries pertaining to the testing and distribution of drugs.

I would like to go into detail in the drug section point by point.

2. (*a*) It is my feeling that the Minister of National Health and Welfare Honourable J. Waldo Monteith, should make a statement pertaining to the terms of reference and give an explanation of the government's policy in this regard.

2. (*b*) The director of the food and drug directorate should explain the particular sections of the Food and Drugs Act and regulations which provide him with the authority to control the introduction of drugs into Canada.

He should explain the administrative procedures which are followed within the directorate to have a new drug released to the public for clinical and general use.

The director should explain the limitations in the existing act and regulations in respect of the control of both new and old drugs, which he feels are lacking.

Differences in the regulations in the United States and Canada in the handling of new drugs should be explained; for example, prescription drugs, research, preclinical requirements, effectiveness data and advertising.

The director should explain any difficulty pertaining to personnel make-up and so on, and perhaps mention any recruiting and understaffing problems.

2. (*c*) Pharmaceutical manufacturers should be asked to present the committee with a report on existing practices in respect of the preclinical testing of drugs. They should be asked to outline the type of preclinical testing which is carried out on various classes of drugs before the drugs go into clinical trials and give an evaluation of the effectiveness of present testing procedures in the prevention of serious side effects in humans during clinical trials, and later when the drug is released for general use.

In their report, they should give a description of how they transmit their information to the druggists and physicians in the country as a whole, with particular reference to their advertising brochures.

In this connection I might mention three names:

Dr. Armand Frappier, Directeur. Institut de Microbiologie et d'Hygiène de l'Université de Montréal, Dr. J. Parker, Director, Research, Chas. E. Frost and Co., Montreal, Dr. J. D. McColl, Director, Pharmacological Research, Frank W. Horner Limited.

There is another list of manufacturers and professional people that your chairman has at his disposal, which can be used to facilitate our investigation.

2. (*d*) Pharmaceutical manufacturers should provide the Committee with a report on these practices in respect of the clinical trials which are carried out in advance of the general release of new drugs. This report should cover at least the following:

(i) Information on their selection of clinical investigators, for example, what is their criteria of acceptability for the selection of qualified investigators?

What part does the manufacturer's representative play in actually planning the clinical trial?

Are these trials carried out in hospitals?

What is the criteria of acceptability for a new drug?

(ii) Any specific recommendations concerning existing legislation on new drugs on which they would like to comment pertaining particularly to the safety element.

There are two names for your consideration here, Dr. K. K. Ferguson, Director, Connaught Laboratories, Toronto, Ontario and Dr. L. Smith, Medical Director, Ayerst, McKenna and Harrison Limited, Montreal, Quebec.

The references are the same as I have read out for section 2 (*c*), pertaining to the other witnesses that may be called.

2. (*e*) Any expert or experts in clinical medicine should be called to give an appraisal of existing requirements respecting the preclinical and clinical testing of drugs before their release for general use. He, or they, should answer such questions relating to, for example, are we doing all that can be done in our preclinical and clinical testing of drugs to safeguard the public and so on?

There are three gentlemen indicated here who are eminent in the field in the United States. I have a list of Canadian people but it is very lengthy and that is why I did not incorporate it in this statement. We have: Dr. J. T. Litchfield, Director, Experimental Therapeutic Research Section, Lederle Laboratories, New York, Dr. J. Holland, Medical Director, American Home Products, New York and Dr. K. K. Chan, Director, Pharmacological Research, Eli Lilly and Company, Indianapolis.

We have an extensive list of eminent doctors and professors in Canada whom the committee may like to consider at a later date.

2. (*f*) Pharmaceutical manufacturers should be requested to present to the committee the various methods which are used to promote the sale of drugs in Canada. Such methods as advertising, labelling and detailing of drugs, and qualifications of drug representatives in the field should be examined by the committee. Consideration of their quality control practices would be advisable.

(i) Canadian Pharmaceutical Manufacturers Association.

(ii) Canadian Pharmaceutical Association.

2. (*g*) It would appear to be advisable to hear from a general practitioner, or practitioners, about the impact of all these various methods of drug promotion on the practice of medicine and whether he or they would have any comment to make on present-day practices in so far as they may effect the safe administration of drugs.

A practicing physician or physicians appointed by the Canadian Medical Association.

2. (*h*) The committee should investigate ways and means of informing the public of the misuse of drugs in the home; for example, making sure that drugs are out of the reach of children; cleaning out medicine cabinets regularly and so on.

Mrs. A. F. W. Plumtre, President, Canadian Association of Consumers, Ottawa.

Information officers of the Department of Health and Welfare should be called.

3. The Chairman of the special committee of the Royal College of Physicians and Surgeons should be called to present to the committee the recommendations in that committee's report. They should inform the committee the reasons for the recommendations which have been made and be expected to answer questions. They will probably require other members of the committee to assist him in answering questions.

Terms of reference of this committee are:

> To examine critically and objectively our present procedures for dealing with new drugs, the requirements of the regulations, and any other matters that, in the opinion of the committee, are relative to the issue. I should point out that the purpose of the new drug regulations is to ensure safety.

Dr. F. S. Brien, Chairman

Dr. E. A. Sellars and Dr. R. Dufresne.

4. In order for the committee to have a better idea of how the sale and marketing of drugs are controlled in other countries, it would be advisable to have someone appear before the committee and outline some of the regulations which are in effect in various countries. The World Health Organization has a unit which deals with standards for pharmaceuticals. The head of the unit should be able to provide the committee with details on existing legislation in various countries and be able to give a limited appraisal of existing legislation.

Mr. Paul Blanc, World Health Organization, Geneva, Switzerland.

The next section of the proposal is a list of professional people, professional associations and individuals that might be called. I do not have the list of manufacturers because the list is as long as your arm and I think we can trust the subcommittee to bring proper proposals before this committee in respect of this aspect. If you like I will go through the list of witnesses that we propose calling for your consideration in these terms and their qualifications or shall I just take it as read?

I think perhaps I should go over them. They are: Dr. A. D. Kelly, General Secretary, The Canadian Medical Association, 150 St. George Street, Toronto 5, Ontario; Mr. J. C. Turnbull, Secretary-Manager, The Canadian Pharmaceutical Association, 221 Victoria Street, Toronto, Ontario; Dr. E. W. Bensley, Secretary, The Pharmacological Society of Canada, Montreal General Hospital, 1650 Cedar Avenue, Montreal, Quebec; Dr. John C. Laidlaw, President, The Canadian Society for Clinical Investigation, 36 Hudson Drive, Toronto, Ontario; Dr. W. W. Tidmarsh, Secretary, The Canadian Paediatric Society, 79 Percival

Avenue, Montreal 28, Quebec; Dr. J. Wendell MacLeod, Secretary, Association of Canadian Medical Colleges, 710 Albert Avenue, Saskatoon, Saskatchewan; Dr. Don. W. Gullett, Secretary-Treasurer, The Canadian Dental Association, 234 St. George Street, Toronto, Ontario; Dr. L. P. E. Choquette, Executive-Secretary, The Canadian Veterinary Medical Association, P.O. Box 416, Ottawa 2, Ontario, and Dr. Georges Filteau, President, College of Pharmacists of Quebec, 1290 St. Denis Street, Montreal, Quebec.

Those are the professional associations that I have listed in the report.

Then we have a list of trade associations as follows: Mrs. A. F. W. Plumtre, President, The Canadian Association of Consumers, 1245 Wellington Street, Ottawa 2, Ontario; Mr. Stanley N. Condor, General Manager, The Canadian Pharmaceutical Manufacturers Association, 301-311 Royal Bank Building, 90 Sparks Street, Ottawa, Ontario.

I will have my French colleague read the last one.

Mr. VALADE: The last one on the list is: M. Jean-Marie Pepin, Secretaire, L'Association des Fabricants du Quebec, de Produits Pharmaceutiques, C.P. 125, Station Youville, Montreal 11, Quebec. That is the Secretary of the Association of Quebec for the manufacturing of drugs.

The CHAIRMAN: I have next a list of the individuals proposed in respect of this section which is as follows: Dean F. N. Hughes, The Faculty of Pharmacy, University of Toronto, 46 Gerrard Street East, Toronto 2, Ontario; Docteur Armand Frappier, Directeur, Institute de Microbiologie et d'Hygiene, de L'Université de Montreal, 2900 Boulevard Du Mont-Royal, Montreal 26, P.Q.; Dr. John F. McCreary, Dean, The Faculty of Medicine, University of British Columbia, Vancouver, B.C.; Dr. K. J. R. Wightman, Professor of Medicine, University of Toronto, 46 Gerrard Street East, Toronto 2, Ontario.

Dr. J. K. W. Ferguson, Connaught Medical Research Laboratories, University of Toronto, Toronto, Ontario; Dr. F. C. Fraser, Professor of Genetics, McGill University, Montreal, Quebec; Dr. John O. Godden, Associate Editor of C.M.A. Journal; Dr. Elizabeth Hillman, Head of Poison Centre of Montreal's Children's Hospital, Montreal, Quebec; Dr. Rabinowitch, P.O. Box 216, Hanover, Ontario; Dr. O. Brzeski, Sandoz Pharmacy Company, Montreal, Quebec; Dr. Hans Selye, Montreal, Quebec; Professor William Boyd, Toronto, Ontario; Dr. J. G. Foulks, University of British Columbia; Dr. E. E. Daniel, University of Alberta; R. Christie, Professor of Medicine at McGill University, Montreal, P.Q.

Dr. Ford, Department of Medicine, University of British Columbia, Dr. McNeil of Calgary, Dr. Roger Dufresne of the special committee of physicians and surgeons, Dr. D. E. Cameron, Allan Memorial Institute of Montreal, Dr. A. Hoffer, University of Saskatchewan, Dr. Tyhurst, University of British Columbia.

That is the first section on drugs, and if you will turn to the end of your report you will see a schedule of meetings that I have prepared for the consideration of the committee. I think that before we get into pesticides, we should go over this agenda so that we can consider safety as a whole.

The following is the schedule of meetings of the special committee on food and drugs: January 24—this morning a general discussion of the report of the chairman of the subcommittee was proposed.

January 29, that is next Tuesday, at 9:30 a.m. it is proposed that the Hon. J. Waldo Monteith, Minister of National Health and Welfare give his statement, followed by Dr. C. A. Morrell, director of the food and drug directorate, Ottawa, pertaining to the policy of the government and the position of the directorate as indicated in the first part of my statement; January 31, 9:30 a.m., a continuation of that discussion.

February 5, 9:30 a.m., it is proposed that members of the special committee of the Royal College of Physicians and Surgeons, drug investigation committee, Dr. S. S. Brien, chairman, Dr. E. A. Sellars, and Dr. R. Dufresne be called to give witness pertaining to their report, which by that time will have been in our hands as I believe it is going to be tabled in the house today.

On February 6, 9:30 a.m. and February 7, 9:30 a.m., we will continue with discussions, if necessary, of the investigation of the committee as I mentioned above.

February 12 and 13, we will visit Montreal to see first hand clinical research and manufacturing facilities, to include units at the Hôtel-Dieu hospital under the directorship of Dr. Jacques Genest, Ayerst, McKenna and Harrison Limited, biological and pharmaceutical chemists, and Charles E. Frosst and Company, and their Kimm laboratories.

February 14—we can have a discussion on that later. I do not think the committee should crowd its hearings because if we bring witnesses from all over the country or from the United States or anywhere else, we should leave ample room in which to give them consideration so that they will not have to stay here for two or three weeks.

Mr. HAIDASZ: Are we going to be allowed to discuss this agenda later?

The CHAIRMAN: Yes; at the end of the discussion I want to throw the whole section open for discussion on drug safety and on the agenda.

February 19, 9:30 a.m., start receiving evidence from professional associations, trade associations and professional individuals, all relating to section "A" of the terms of reference. "The law and practices relating to the control of the introduction, marketing and use of drugs." (safety)

February 26, 9:30 a.m., Mr. Paul Blanc, World Health Organization, Geneva, Switzerland who has kindly consented to come that week, if we want him to.

Meetings in future will be determined at a later date.

Can we now have a discussion on the agenda as outlined? The reason we kept the special associations and professional people off until February 19 is that we wanted the permission of this committee to notify all the proposed witnesses of our intention to ask them, thereby giving them ample time to prepare their statements or reports to this committee. We thought that by having the departmental officials and the special committee of the Royal College of Physicians and Surgeons, first we would do this in a very orderly way. Could we have a discussion of the schedule, or would you like an over-all discussion of the drug situation?

Mr. MITCHELL: If I might intervene here for a moment, when you spoke of government officials I noticed that R. C. Hammond was not included in your group. As you know, he is the director of narcotic control, and under his direction are the special schedule G drugs. This is very necessary for this committee's information.

The CHAIRMAN: This was discussed, and I did not propose a list of all the people within the Department of National Health and Welfare pertaining to this problem because I thought that when the minister made a statement he would have all the people pertaining to every section of the legislation under his administration with him and they could give us a list of the people that are necessary to investigate this problem completely.

Mr. MITCHELL: He would be included under the food and drug directorate.

Mr. HAIDASZ: I was just going to make a statement on the schedule of meetings, and specifically the meetings scheduled for February 12 and 13—visits to Montreal.

The CHAIRMAN: If I might interrupt, this has not been actually scheduled; I have just made some preliminary phone calls and suggested certain dates which can be changed at the wish of the committee. I wanted to do it in an orderly way.

Mr. HAIDASZ: Members of the Liberal party on this committee would be attending the annual meeting of the advisory council of the National Liberal Federation on February 12, therefore February 12 would not be a suitable date for us.

The CHAIRMAN: Might I suggest then, if it is the wish of all the members of this committee, that we could transfer the date from February 12 to February 13 and 14, in other words, we would transfer the date to Wednesday and Thursday, and this would get away from any change. We could change this easily to another week.

Mr. HARLEY: There are other things on February 13. Could we make it February 14 and 15?

The CHAIRMAN: I am in the hands of the committee. The only reason these dates were announced in the report is that I talked to these people about a certain date. We can have it any day or week you want. Is it convenient for the members of the Liberal party to come on February 13 and 14?

Mr. NICHOLSON: If we are tied up on February 11 and 12 it would seem to me that rather than go down on the evening of February 12 it would be better to go down on February 14 and 15.

The CHAIRMAN: Is it agreeable to the committee that we go to Montreal—and we must ask permission of the house to do this—on February 14 and 15 instead of February 12 and 13?

Mr. FAIRWEATHER: There is no Place Pigalle in Montreal.

The CHAIRMAN: We will not have to worry.

Mr. FAIRWEATHER: These kind people are safe.

Mr. HARLEY: I did not have time to go through the complete list of witnesses as far as their qualifications are concerned. I was thinking particularly of drugs. Was there any thought of calling someone who might be an organic chemist not connected with a drug organization?

The CHAIRMAN: Yes, at the end of the whole statement I wrote a paragraph—I probably got ahead of myself—where any person that the committee wants in an unbiased way, in other words not associated with a manufacturer or a research institute for profit, should be called by the committee, and if any members of the committee have witnesses they wish to call, please submit their names.

Mr. HARLEY: I was thinking of an organic chemist and a biologist.

The CHAIRMAN: Have you a name?

Mr. HARLEY: Not offhand. The only organic chemist I can think of is Professor Rogers of the University of Toronto.

The CHAIRMAN: I will have a list, prepared by the department, of eminent men in that field so that the subcommittee or the committee can consider it.

Mr. BALDWIN: Mr. Chairman, first I would like to compliment the chairman and those members of the subcommittee who have so painstakingly and thoroughly prepared this report. I think it will make our task a lot easier. It indicates an excellent series of meetings.

I would like to make the suggestion that this is a matter of which we have had some inkling in the proceedings in the House of Commons already. I refer to the matter of control. I think this will be particularly so when we

come to deal with the second branch of our inquiry, namely, pesticides, insecticides and so on; and, judging from what you have said, we shall be making most careful inquiry into the existing situation, bearing in mind that we will be making certain recommendations.

That brings up the question of just how far, in a divided federal jurisdiction, we, as the parliament of Canada, are going to be able to make suggestions which will be valid. I suggest that we might consider calling—if the committee so wishes—somebody from the Department of Justice. I think this should be done at the latter part of the proceedings, and it should be someone who would be able to tell us on what basis the present Food and Drugs Act rests, and on what basis the establishment and legality of any recommendations we make in the future will rest; and at the same time, we should bear in bind that provincial governments all have some jurisdiction as well. This might give us some indication as to what steps have been taken by the provincial governments along the lines into which we are making inquiry.

The CHAIRMAN: We shall check into that and have it put on the agenda, if it is the pleasure of the committee.

Mr. MITCHELL: I would like to commend the committee on accepting the invitation to go to visit those two pharmaceutical manufacturing plants in Montreal. It is not particularly new to some of us on this committee, but it will be particularly new, and very interesting, for those who have never had that opportunity. It should also satisfy some of the questions which might be asked about the subject of control of pharmaceutical preparations and of other chemicals through to their being found in marketable form. I think it should serve to answer some of the questions which might be asked.

Mr. NICHOLSON: I am also very pleased to see that the visits to these manufacturing plants are included. I wonder if, in the course of our visit to Montreal, we might include a visit to a proposed pharmaceutical manufacturer whose background is not purely Canadian, but more that of North America. I have in mind Ciba, whose parent office is in Switzerland, or something of that kind.

The CHAIRMAN: We will take a note of that for consideration by the committee. The only problem of this visit is that it means that for two days, to be visiting these three people that we recommend initially, we would have to be running around the place. If we crowd in too many people in that two-day visit I do not think we would get any value out of the investigation. But if the committee wishes to make the visit at some particular time, I think it might be in order for us to go.

Mr. NICHOLSON: I know something about the chemical industry and of the differences which exist between Canada and Europe, and the United States and Europe in that regard.

The CHAIRMAN: Would you give me your permission to investigate this, Mr. Nicholson, and I shall report on it at the next meeting?

Mr. HORNER (*Jasper-Edson*): I think a lot of these European companies do not have full manufacturing facilities in Canada, but I have in mind one of them which may do all its North American testing in Canada. I think it is Ayerst, McKenna and Harrison Ltd.

Mr. MITCHELL: I think the European companies with branches in Canada and the United States would be more in the way of packaging operations than that of test control.

Mr. VALADE: May I ask of a question of Mr. Nicholson for clarification? Are you talking about the rough material, the production of raw material which goes into chemicals and pharmaceuticals?

Mr. NICHOLSON: Yes.

The CHAIRMAN: May I go on to the next section. I mean the terms of reference. Section (B) reads: "The dangers arising from contamination of food by the use of chemicals to kill weeds, insects and other pests".

1. "Chairman's Remarks." Well, I have made my remarks at the first of this meeting.

2. Control of pesticide residues in foods under the Food and Drugs Act and Regulations.

3. Registration and control of pesticides under the Pest Control Products Act.

4. Role of the provincial entomologist in the use of pesticides.

5. The toxicological testing of pesticides prior to use.

6. Industrial and commercial evaluation pertaining to development of pesticides.

7. The need for the use of pesticides in agricultural production.

8. Current agricultural practices relating to the use of pesticides in Canada and trends for the future.

1. I have already made my remarks.

2. (*a*), statements of the Minister of Health and Welfare, the Honourable J. Waldo Monteith, and the Deputy Minister of National Health and Welfare, Dr. G. D. W. Cameron, or any other interested people we have pertaining to the responsibility of the government and with reference to the health and welfare department in this regard.

2. (*b*) The director of the food and drug directorate should outline the basic legislation and the regulations which have a bearing on the control of pesticide residues in foods. The administrative procedures followed in handling of a submission regarding a pesticide and the division of responsibility between the Department of Agriculture and the directorate in the handling of such submissions, should be discussed. The information required for the establishment of a tolerance for residues of a pesticide in foods should be given as well as the procedures employed in arriving at a satisfactory level, and future safety in years to come. Terms such as toxicity, hazard, acceptable daily intake, permissible level and tolerance should be carefully explained.

A statement of the number of tolerances established and the pesticides which are permitted on a no residue basis should be provided as well as the number of crops involved. Problems relating to methods of determination of the pesticide residues should be discussed.

Results of surveys of pesticide residues in food in Canada, the action taken when excessive residues are encountered, the manpower available to the directorate for this work and the type of investigation currently underway by the department should be discussed.

Dr. C. A. Morrell, food and drug directorate, director, Department of National Health and Welfare, or any other person we deem necessary, or that Dr. Morrell would like to bring with him.

3. A representative of the Department of Agriculture should be called to explain their responsibilities under the Pest Control Products Act. This should include the information required for registration, division of responsibility between Department of Agriculture and the food and drug directorate. Labelling requirements including all advertising material re warning statements and antidotes should also be explained.

The department should also give the number of registrations under the act, and the effectiveness of the present legislation.

Mr. S. C. Barry, deputy minister of agriculture.

Mr. R. C. Phillips, director, plant products division, Department of Agriculture, Ottawa.

Mr. C. H. Jefferson, chief, feed, fertilizer and pesticide section, plant products division, Canada Department of Agriculture, Ottawa.

4. A provincial entomologist should explain his role in the development of the provincial spray calendars and the basis on which decisions regarding recommendations for use of specific pesticides are reached.

Professor Harold Gobles, provincial entomologist for Ontario, entomology department, federated colleges, Guelph, Ontario.

5. A toxicologist could explain to the committee the toxicological testing required on pesticides before they are considered for use on agricultural crops. He should be asked such questions as to the validity of animal tests in relationship to the safety factor in humans, the adequacy of such tests and related problems.

Dr. Julius M. Coon, Professor of Pharmacology, The Jefferson Medical College, Philadelphia, Pennsylvania. (Chairman of the subcommittee on toxicology, food protection committee, national research council, Washington, D.C.)

6. A representative of the agricultural chemicals industry should be called before the committee to outline the procedures which they employ in the development and testing of a pesticide.

This testimony should include a discussion of toxicity tests conducted on experimental animals and the field tests carried out on a pesticide.

The Canadian Agricultural Chemicals Association could be asked to suggest a representative of their industry.

7. There should be an extensive discussion on the use and need for pesticides in agriculture. A competent agricultural scientist should be called to discuss this aspect of the problem—Dr. D. A. Chant, officer-in-charge, entomology laboratory, Canadian Department of Agriculture, Vineland, Ontario.

8. An agricultural scientist with a broad knowledge of the use of pesticides should be asked to discuss current agricultural practices in Canada. He should be asked to discuss alternatives such as biological control of insects and other pests as well as trends for the future.

He should also be asked if there are any papers or information at his disposal relating to studies carried out by foreign governments in this field.

Dr. Henry Hurtig, associate director, pesticides, programme directorate, research branch, Canadian Department of Agriculture, Ottawa.

Dr. Robert Glen, assistant deputy minister, research branch, Canadian Department of Agriculture, Ottawa.

There are a good many other persons in this field who could be called. I anticipate this question being asked: There are writers of books such as Rachel Carson who take a very extreme view, and I think all members of the committee should avail themselves of the opportunity of reading those books.

Eminent men in the fields of pharmacology, therapeutics and chemistry should be called to give evidence in relation to the possible harmful effects on the human body in the use of insecticides, and recommendations to minimize these harmful effects, if any.

There is a list I have prepared. It is not complete because I did not have an opportunity to get the companies. However, I will go over it briefly. The professional associations include the following:

Dr. E. H. Bensley, secretary, The Pharmacological Society of Canada, Montreal General Hospital, 1650 Cedar Avenue, Montreal, Que.

Dr. A. D. Kelly, general secretary, The Canadian Medical Association, 150 St. George Street, Toronto 5, Ontario.

Mr. P. H. G. Michael, general manager, Canadian Institute of Chemistry, 48 Rideau Street, Ottawa, Ontario.

Mr. J. E. McConnell, executive secretary, Agricultural Institute of Canada, 176 Gloucester Street, Ottawa 4, Ontario.

Then the trade associations:

Mr. Michel Chevalier, general manager, Canadian Agricultural Chemicals Association, 3405 Cote des Neiges Road, Montreal 25, P.Q.

Mr. W. K. St. John, executive secretary, National Dairy Council of Canada, Room 305, The Journal Building, Ottawa, Ontario.

Mrs. A. F. W. Plumptre, president, Canadian Association of Consumers, 1245 Wellington Street, Ottawa 3, Ontario.

Mr. John Monkhouse, executive secretary, Dairy Farmers of Canada, 147 Davenport Road, Toronto, Ontario.

The individuals include Dr. Mark Nickerson, Faculty of Medicine, Department of Pharmacology and Therapeutics, University of Manitoba, Winnipeg, Manitoba.

There are some other persons such as Rachel Carson, and although I do not have her proper title I remember her name in the book. There are no lists here of the chemical manufacturers. It is my understanding, in discussion with the agricultural section of the federal government, that a great many of the raw chemicals used in pesticides are manufactured in the United States and imported into Canada. I have asked that they prepare a list of the major manufacturers, the people to whom they sell their products, and how they go into the process. This will be a complete list so that the committee can scrupulously go through it.

I think this committee as a whole should recommend the names of any persons they might like to call in the field of pharmacology, therapeutics and chemistry in this regard.

Mr. NICHOLSON: I would like to join with Mr. Baldwin and Mr. Mitchell in complimenting you, Mr. Chairman, and the steering committee—more particularly yourself—on this very excellent memorandum which has been prepared.

It does seem to me that there is another part of the federal government which should be brought into this part of the study; that is the Department of Forestry. We spend millions of dollars a year in British Columbia—hundreds of thousands—in large wholesale spraying of forests for the purpose of killing insects. That has an effect on the food, not only because of the berries, but also the fish and wild life. I think in many ways the forestry department is almost as important as the agricultural department.

The CHAIRMAN: I thank you very much for bringing that to our attention. At our meeting the doctor in charge of research in the agriculture department did mention this. There are the soil conservation people, the cross breeding of agricultural products, and the people pertaining to wood products and wild life.

Mr. NICHOLSON: This is more than that. There is a special committee in British Columbia made up of representatives of the federal government, the department of forestry of the province and the department of lands and mines of the province as well as industry. They take a whole section of Vancouver

Island and the mainland and spray the area. They are, and have been for some time studying the effect on fish life, food, agriculture and other things. This spraying extends over miles.

The CHAIRMAN: Mr. Nicholson, might I say that in preparing the agenda in respect of this subject matter I have the permission of the committee to call the Minister of Forestry and his officials. This could be incorporated in the agenda.

Mr. FAIRWEATHER: In New Brunswick the same situation pertains. In one instance the federal Department of Fisheries sued a crown corporation. It was a joint federal, provincial and pulp and paper company venture. The fisheries department lost a lot of fingerling salmon as a result of spruce budworm spraying. There is some balance there and it may be interesting to hear the philosophy of the balance.

The CHAIRMAN: I think if Mr. Nicholson's suggestion could be adhered to we could bring in both agriculture and forestry, and in that way I think we can do things properly.

Mr. NICHOLSON: I think there is an assistant deputy minister who has a broad background of experience in respect of the tests for the control of the budworm and other insects. I am inclined to think that this assistant deputy minister or the director in charge of this branch might be more helpful rather than the minister.

The CHAIRMAN: It is anticipated that we will be discussing the aspect of the government's responsibility and therefore initially should call the minister to give a statement. Then we might have the officials of the department who are necessary in helping us complete our investigation.

Mr. RYNARD: I am wondering, Mr. Chairman, if we should follow Mr. Baldwin's suggestion and have someone from the Department of Justice so that we might have his views in respect of the various things we can do. Take, for instance, the department of lands and forests. In the province of Ontario that department is under the provincial government, and perhaps we should have their field clearly defined before we start into a federal program which may interfere with a provincial program. Let us know what our fields are. I think it might be worth while to have that made plain before we get too deeply into the matter.

The CHAIRMAN: Is there any discussion on that point?

Is it the wish of the committee that I get in touch with the Department of Justice in order to have someone prepare a statement in respect of the responsibility of this committee pertaining to the division of responsibility between the federal and the provincial governments?

Mr. FAIRWEATHER: Not if we are to be restricted.

The CHAIRMAN: No. It is not our intention that this committee is to be restricted.

Mr. VALADE: I think this committee is involved with investigating into the history and use of drugs and pesticides; we are not going to impose on any legislative or provincial jurisdiction. As a fact-finding committee I think it does not matter whether it is a provincial or federal jurisdiction. We just want to bring out the problem and, after that, the responsibility would be shared by the provincial or federal government, if it comes to a solution.

The CHAIRMAN: Is it the wish of the committee that a departmental official from the Justice Department be called to give an explanation or should we reserve this for the latter part of our hearings.

Mr. RYNARD: My thought, Mr. Chairman, was not to have any interference whatsoever. It was just so that we would know what the situation was legally. I hope I did not intimate that there should be any restrictions applied at all.

Mr. VALADE: Do you think we should call these people when we come to the recommendations of the committee at the end of our hearings? Is it the wish of the members of the committee to request their advice on this? Would that be all right?

Mr. RYNARD: It is all right. My feeling is that if we know beforehand just what the situation is we can go ahead and make recommendations.

Mr. VALADE: I am worrying about having the statement made before we start our inquiry. If we do we might be involved in some restrictions insofar as investigation is concerned.

Mr. BALDWIN: It is my suggestion that we have a very brief statement from someone from the Department of Justice along the line Dr. Rynard suggested before we deliberate and propose recommendations. However, I feel the same as anyone else, namely, that the deliberations here should be completely exhaustive and we should cover everything whether under our jurisdiction or not. When we come to make suggestions later on, then I think there should be a great interest shown not only on the part of our federal government but on the part of provincial governments as well as to where the responsibility might lie, and then at the latter part of our proceedings we might call in a representative from the Department of Justice if we think it is necessary at that time.

The CHAIRMAN: Is it the wish of the committee that I have the Department of Justice make a short statement or should we have a lengthy statement at the end before we make our recommendations.

Hon. MEMBERS: Agreed.

The CHAIRMAN: Is there any further discussion in connection with the pesticides section?

Mr. HORNER (*Jasper-Edson*): Mr. Chairman, I have in mind one section which has not been mentioned today and which I think is very important to us, particularly in Western Canada. It has to do with the grain trade, the use of pesticides and the residue in grain particularly, not only for domestic consumption but export consumption. This is vitally important to us and it is at the fore in Western Canada at the moment. I suggest that Mr. Connacher, chief testing officer in the board of grain commissioners be one of our witnesses. As well, it would be of great assistance to us if we could have from the Department of Agriculture the veterinary director general.

The CHAIRMAN: Is there any other discussion in connection with the pesticides section? If not, I will go on to the next section, namely prices and costs.

I anticipated there might be a problem in this regard and I would like to read out again what the minister said in the House of Commons on December 7 at page 2442 of *Hansard,* at which time he was replying to the suggestion that this committee investigate the cost of drugs. He said:

> Mr. Speaker, in closing this debate I should like to point out that I think it is probably up to the committee itself to determine the definition of the word "marketing" in the resolution.

Since my appointment as your chairman, on December 19 I have given considerable attention to this and it is my feeling that the prime objective of this committee is the safety factor—and this was the intention of the government. However, the minister, as you will note, did give us an opening in the wording of this to discuss certain situations pertaining to the costs. As your chairman I would not want the safety aspect to get thrown into the background because I think it is the most important thing that faces this country today. We probably will have reference to the thalidomide tragedy and so on, and if we confuse the two initially we will get into trouble later on. I think we

should start our hearings on the drug safety factor and leave in abeyance consideration of the cost factor until after the restrictive trade practices commission reports. Members of this committee will be supplied with copies of this report.

The thing that I fear from the legal aspect is that many people who may be named in this report might be charged under their terms of reference and might incriminate themselves by coming before this committee and testifying on the cost of drugs. It is my opinion that if we mix up safety and the price factors or costing we will not cover what the terms of reference adequately state.

I would like to have the unanimous consent of the committee to defer the complete discussion on this section until later on—without hampering the committee in anyway—thereby leaving the matter open until the restrictive trade practices report—on which Dr. Haidasz posed a question in the house yesterday—is tabled. We were given to understand that this would be forthcoming shortly, which would be about in three weeks time, I think.

Mr. FAIRWEATHER: Mr. Chairman, I think there is another feature in connection with the costs; the royal commission on health has had exhaustive evidence on this matter and, of course, their report is expected soon.

The CHAIRMAN: If I might interrupt, Mr. Fairweather, I had another section to cover before completing my remarks.

I was going to suggest that a great many briefs were presented to the royal commission on health services pertaining to the costs and although I do not wish to hamper this committee my view is that the safety factor is of prime importance. I would ask that we delay any decision in connection with costs as interpreted in the word "marketing" in the terms of reference until after the restrictive trade practices report. If we proceeded in this way I think we would serve the purpose of this committee better.

Mr. NICHOLSON: I noticed, Mr. Chairman, that there is no reference to proprietary and patent medicines. I have received a number of telephone calls in Vancouver on this subject requesting that we discuss it. I was in receipt of these calls owing to the fact perhaps that I was the only one on the committee from British Columbia.

The CHAIRMAN: Dr. Morrell and I have had discussions with about 30 people in getting together my information. Dr. Morrell is going to clarify his position with regard to the control of drugs and at the same time I think he is going to make a reference to patent medicines and whose responsibility it is, throughout the manufacture and research into these medicines. It was the intention of the chairman perhaps to call people that do the importing of these patent medicines to prove their clinical responsibility in that regard.

Mr. MITCHELL: Mr. Paul Soucy is the gentleman in charge of proprietary and patent medicines as far as the Department of National Health and Welfare is concerned. He is in Dr. Morrell's department and I am sure he would be available to answer any questions.

The CHAIRMAN: In outlining the first section I did not want to go into too much detail and that is why I approached the chief person involved in each of these sections. However, this committee can call anyone it sees fit to call.

Are there any further discussions on the three sections we have covered?

Mr. HAIDASZ: Mr. Chairman, I think that the formation of this committee is a direct result of the thalidomide tragedy. In view of that fact I feel that the company which introduced thalidomide into Canada should be permitted to present a view following whatever evidence may be given to us by the officials of the Department of National Health and Welfare. I was wondering

whether you had given notification of these hearings to that company or whether someone from that company had notified you of their intention to appear before this committee.

The CHAIRMAN: I might say, Dr. Haidasz, that I did not want to officially write anyone until this committee had given me permission to do so, although I have received telephone calls from many manufacturers and associations.

No one from the William S. Merrell Company has telephoned or written to me, but it was the intention of your chairman to write letters to professional associations and manufacturers, professional people and research people indicating that we propose to call them at some future date in order to give them ample notice. I might say that the Merrell company was on my list of manufacturing companies to be notified. I did not include the complete list in this statement because of its length. If any members of this committee wish individuals called or companies notified other than those I have listed, I should be very pleased to have an indication in this regard.

Mr. RYNARD: Mr. Chairman, I am in agreement with Dr. Haidasz' suggestion that someone from the Merrell company be called, and I would also like to suggest that Dr. Fraser be called as soon as possible because of the fact he is an outstanding man in the genetics field.

As Dr. Haidasz has indicated, the thalidomide tragedy is the actual cause of the formation of this committee and in that regard I think someone from the Merrell company and Dr. Fraser should be called as quickly as possible.

Mr. NICHOLSON: Mr. Chairman, I should like to make one other suggestion. You have suggested in your report that we call one or more general practitioners. I am wondering also about the many articles that have appeared in *Macleans'* Magazine and other places, and whether it would be advisable to call as well as one or more general practitioners, one or more paediatricians because of the fact children are involved.

The CHAIRMAN: That is exactly why Dr. W. W. Tidmarsh, Secretary of the Canadian Paediatric Society is to be called, and it is presumed that he will bring people with him who are specialists in this field.

Mr. HARLEY: I was pleased to hear Dr. Haidasz refer to the thalidomide question. I think it should be pointed out to the individuals of the company responsible for the introduction of thalidomide into Canada that it is not our intention in having them appear before us to place them on trial or to give them the opportunity of exonerating themselves, but for the purpose of providing this committee with information in respect of the handling of drugs of this type in order that some measure can be taken to prevent any possible further tragedy.

The second item upon which I should like to touch has reference to the statement in the House of Commons regarding pesticides. There is one aspect of this matter in respect of agriculture that has not been mentioned and which I think probably should be mentioned. That is the use of drugs for cattle, which is not really considered dangerous, but which gives rise to contamination through feeding or the use of chemicals for killing weeds and pests. I have reference to drugs and several antibiotics that are used for the purposes of fattening cattle. I think this is a very important aspect that should be considered thoroughly. It is my understanding that certain drugs are being injected into cattle before they are killed which are supposed to be meat tenderizers. This is another aspect which I think should be considered.

Mr. HAIDASZ: I believe that one of our terms of reference covers a study of food additives especially in relation to baby foods.

The CHAIRMAN: I must apologize, Dr. Haidasz, for not bringing the list which you sent me, although I might mention that you did send a letter to me listing all those companies that you felt should be asked to appear.

Mr. HAIDASZ: I feel that as well as calling representatives from the companies which manufacture food additives, particularly in respect of children's foods, we should also have representatives appear from companies that have made available in Canada the drug known as L.S.D., namely the Sandoz company, in order to air the complaints made by the various psychiatrists in clinical research in respect of alcoholism and schizophrenia. I feel, therefore we should call some represenative from the Sandoz company.

Mr. BALDWIN: Mr. Chairman, I might point out in respect of the question raised by Dr. Harley that the definition of the word "drug" itself in the act refers also to drugs used in connection with animals or human beings.

Mr. HARLEY: It was my suggestion that the drugs used for meat tenderizing and for the fattening of cattle, such as hormones, would not be covered.

Mr. HORNER (*Jasper-Edson*): Mr. Chairman, I think these are all covered in the act.

Mr. HARLEY: What does the chairman visualize as our hours of sitting?

The CHAIRMAN: This chairman visualizes a long session. It was our thought that we would meet regularly on Tuesdays and Thursdays at 9.30 in the morning and sit until 12 or 12.30. We also thought that if it was the desire of the committee to complete the evidence of a witness we should sit after orders of the day until perhaps 5.30, using Wednesday mornings from 9.30 until 10.30 in order to complete a witness's testimony of the previous day. It is also our feeling that we should deal with the drugs section first, complete that, and then consider the second section in respect of contamination of foods and insecticides.

Mr. HARLEY: I take it there would be no objection to questioning one witness in relation to the second section even though the witness was called in respect of the first section?

The CHAIRMAN: I think that will be satisfactory providing that we do not become side-tracked and involved in an extensive discussion resulting in a loss of the main theme of continuity. I do not foresee any problem in this regard.

Mr. BALDWIN: Although most witnesses will probably do so, it might be suggested to them that they prepare and send briefs to us so that we can follow the briefs at the time they are presenting their evidence. I think this practice is a very useful one. They should, of course, be informed that they will be allowed to expand upon the remarks contained in the brief.

Mr. FAIRWEATHER: I think that is a good suggestion providing we do not follow the practice of allowing the witnesses to read their long briefs. We can all read, or at least that is the assumption.

The CHAIRMAN: I think we will find that individuals representing trade and professional associations appearing before this committee will have briefs, although perhaps certain biologists, chemists, pharmacologists and professional people from universities and independent laboratories may not present briefs. They will, of course, be called on to explain their positions in respect of certain fields. I will, however, indicate in my letters to these companies and professional peoples that it would be preferable that they submit briefs to this committee before their appearance.

Mr. HORNER (*Jasper-Edson*): Mr. Chairman, one of my colleagues happens to be the medical director of S.K. and F. and has offered the use of a film in respect of the Kefauver inquiry into drugs in the United States. It is about one half hour in length. He has suggested that perhaps this committee would like to see this film and, if so, he will make it available.

The CHAIRMAN: What is the pleasure of the committee in regard to this situation?

Mr. NICHOLSON: Mr. Chairman, I wonder whether Dr. Horner has seen that film.

Mr. HORNER (*Jasper-Edson*): No, I have not, Mr. Chairman.

The CHAIRMAN: It is my opinion that the steering committee should take this suggestion under advisement and bring a report to this committee after finding out what this film contains. Certainly an extensive discussion in respect of the Kefauver anti-trust study in the United States would hamper us in our progress.

Mr. MITCHELL: Mr. Chairman, I have a copy of Senator Kefauver's amendment to the United States federal food and drug act which was presented by him at NATO last November. I happened to be on that committee and I have it in my files. It would be available any time you want to refer to it.

The CHAIRMAN: I may point out that the special committee of the Royal College of Physicians and Surgeons in their report, I understand indicated that they did make a visit to Washington to consider the safety aspect. I think that before we give any consideration to calling any witness from Washington at the government level we should hear them first so that they would not have to go through external affairs and get into a great deal of difficulty.

Mr. VALADE: I do not think the committee has been empowered to have French copies printed.

The CHAIRMAN: It will be done in order.

Mr. VALADE: In the interest of this committee we should have it done.

The CHAIRMAN: I have a list of correspondence, copies of which I will file with the clerk of the committee. These are letters I received from manufacturers associations, consumer associations, manufacturers of drugs, French associations in the province of Quebec, microbiologists, and interested people. Rather than read them all out, I will file them with the clerk of the committee and have a photostat made of them so that we will have a file on all the correspondence.

We require a motion to determine how many copies of the evidence in English and French are required.

Mr. MITCHELL: What is the usual number, is it 750 English and 250 French?

The CHAIRMAN: As the clerk advises me, it depends on the interest. I would suggest that we have initially 750 in English and 500 in French, or maybe even the same number in French because a lot of the people who are going to be called before this committee have indicated to me that they would like to keep complete documentation of what is going on in the committee so that when they do come they can serve a better purpose.

Mr. VALADE: I will move that an equal number of French and English copies be made available, and that the number be 750 of each.

The CHAIRMAN: Is it the pleasure of the committee to adopt this motion? It is seconded by Mr. Horner. All in favour? Opposed, if any?

Motion agreed to.

The only other problem will be that if we go to Montreal on that date we must seek permission of the house to have our actual sittings take place in Montreal. If we do not do this it will just be an unofficial journey, and I think it should be an official journey. If I have permission of the committee, I would like to ask this from the house. That is agreed.

Mr. NICHOLSON: Since February 14 and 15 are Thursday and Friday, might it not be wise, in case you needed to extend the visit to Saturday, to make provision to do so rather than have to make another trip down there? We are going to visits plants and factories.

The CHAIRMAN: I will be frank with you. In talking to the people in Montreal they said they would like us to come on Wednesday afternoon and use Wednesday afternoon, Wednesday night, Thursday and Friday. I anticipated some difficulty in the Wednesday night situation, as has been indicated in the house, and that is why I did not do it. I myself would prefer to have Wednesday afternoon, Thursday and Friday, but if you want to have Saturday morning, it does not matter.

Mr. MITCHELL: Mr. Chairman, what is the opposition to Wednesday evening?

The CHAIRMAN: There was no opposition except that there is a Liberal meeting on Sunday, Monday and Tuesday, and they did not want to crowd things. They also have correspondence to look after.

Mr. RYNARD: Why not arrange it for next week?

The CHAIRMAN: Except that the following week is the only week that the representative of the world health organization is available. If we could not get him, then it would be three months before we could get him again. Thursday, Friday and Saturday is fine with me.

The VICE-CHAIRMAN (*Mr. Valade*): The only point here is that production does not go on in some of the firms on Saturdays, and you may not see the operation.

Mr. NICHOLSON: Some of them operate continuously.

The CHAIRMAN: Some of the people I spoke to in Montreal indicated that they did not operate on Saturdays, and that was the reason we took the middle of the week. What is the pleasure of the committee, should it be Thursday afternoon, Friday and Saturday, or Thursday, Friday and Saturday morning?

Mr. NICHOLSON: Thursday, Friday and Saturday morning.

The CHAIRMAN: I will look after that.

Is there any other business we would like to bring before the committee? Can I have a motion for adjournment? It is seconded by Mr. Mitchell.

We will adjourn until next Tuesday at 9:30 a.m.

OFFICIAL REPORT OF PROCEEDINGS AND EVIDENCE

This edition of the Minutes of Proceedings and Evidence contains the text of Evidence in the language in which it was given, and a translation in English of the French texts printed in the Evidence.

HOUSE OF COMMONS

First Session—Twenty-fifth Parliament

1962-1963

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. R. M. T. McDONALD

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 2

TUESDAY, JANUARY 29, 1963

WITNESSES:

The Honourable J. Waldo Monteith, Minister of National Health and Welfare; Dr. G. D. W. Cameron, Deputy Minister of National Health; Dr. C. A. Morrell, Chief of the Food and Drug Directorate; Mr. R. E. Curran, Legal Advisor of the Department of National Health and Welfare; Dr. L. I. Pugsley, Associate Director of the Food and Drug Directorate; and Mr. R. C. Hammond, Chief of the Narcotic Control Division, Food and Drug Directorate.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1963

28311-9—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. R. M. T. McDonald

Vice-Chairman: Mr. Georges Valade

and Messrs.

Baldwin	Harley	Mitchell
Enns	Horner (*Jasper-Edson*)	Nicholson
Fairweather	Marcoux	Orlikow
Haidasz	Martin (*Essex East*)	Patterson
		Rynard—15

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

MINUTES OF PROCEEDINGS

TUESDAY, January 29, 1963.
(3)

The Special Committee on Food and Drugs met at 9.35 a.m. this day, the Chairman, Mr. R. M. T. McDonald, presiding.

Members present: Messrs. Baldwin, Enns, Fairweather, Haidasz, Harley, Horner (*Jasper-Edson*), Martin (*Essex East*), McDonald (*Hamilton South*), Nicholson, Orlikow, Patterson, Rynard, and Valade. (13).

In attendance: The Honourable J. Waldo Monteith, Minister of National Health and Welfare; Dr. G. D. W. Cameron, Deputy Minister of National Health; Mr. R. E. Curran, Legal Adviser, Department of National Health and Welfare; Mr. Eric Preston, Chief of Personnel Services, Department of National Health and Welfare; *from the Food and Drug Directorate*: Dr. C. A. Morrell, Director; L. I. Pugsley, Associate Director; Dr. R. A. Chapman, Assistant Director in Charge of Scientific Services; Dr. J. B. Murphy, Chief Medical Officer; Mr. M. G. Allmark, Chief of the Pharmacology and Toxicology Section; Mr. Paul Soucy, Chief of the Proprietary or Patent Medicines Section; and Mr. R. C. Hammond, Chief of the Narcotic Control Division.

The Chairman opened the meeting and informed the Committee that the dates of the proposed meetings in Montreal have been set for February the 14th, 15th, and possibly the 16th.

He invited the Minister of National Health and Welfare to address the Committee.

Mr. Monteith introduced the officials of his department who were in attendance. He read a statement, copies of which were distributed to the members, and he answered questions thereon.

At the conclusion of the Minister's remarks and the questioning thereon, Dr. Morrell presented a brief respecting the "Procedures for Examination of New Drug Submissions required by the Food and Drug Regulations" and, at the request of some members, he gave explanations as he went along.

Copy of Dr. Morrell's statement together with a chart showing the establishment of the Food and Drug Directorate were distributed to the members of the Committee, the witness being examined thereon. Dr. Morrell answered questions about the number of new drug submissions made annually, the requirements of the law, the definition of "qualified investigators", etc. He was assisted by the officials of the Department of National Health and Welfare and of the Food and Drug Directorate.

A copy of the Food and Drugs Act was also distributed to each Member.

The Minister gave a short statement on the status of the discussions carried with the provinces in regard to the rehabilitation of thalidomide babies. Assisted by Dr. Cameron, he answered various questions.

On motion of Mr. Fairweather, seconded by Mr. Horner,

Ordered,—That the Chart of the establishment of the Food and Drug Directorate be included in today's record. (*See Appendix "A"*).

On motion of Mr. Nicholson, seconded by Mr. Harley,

28311-9—1½

Resolved,—That the number of printed copies of the Committee's Minutes of Proceedings and Evidence in English including Issue No. 1 be increased from 750 to 1500, and that a sufficient number of copies be made available to the Chairman of the Committee for mailing purposes.

On motion of Mr. Orlikow, seconded by Mr. Horner,

Resolved,—That permission be sought from the House for the Committee to meet in Montreal, Quebec, on Thursday, Friday and Saturday, February 14, 15 and 16, 1963, and that the Clerk of the Committee accompany the Committee to Montreal.

The Chairman announced that the Committee would continue its hearing of the Minister and the departmental officials at the next meeting.

On motion of Mr. Nicholson, at 12.30 p.m. the Committee adjourned to Thursday, January 31st, at 9.30 a.m.

Gabrielle Savard,
Clerk of the Committee.

EVIDENCE

TUESDAY, January 29, 1963.

The CHAIRMAN: Gentlemen I see a quorum.

Before we start I should like to inform this committee that I have been in touch with the people in Montreal concerning the trip. It has been changed to Thursday, Friday and Saturday mornings, February 14, 15 and 16.

Also, Dr. Brien's special committee on new drugs will be here next Tuesday morning at 9.30. I talked to Dr. Brien on the telephone and we are endeavouring to get in touch with the other two gentlemen of that committee to make sure that they can be here at that same time.

I felt this morning, if it is in accordance with the committee's wishes, that we would hear the minister and then ask any questions we have in respect of his statement; then hear from Dr. Morrell, the director of the food and drugs directorate, and then question him in regard to his statement. I hope that is in accordance with the committee's wishes.

Some Hon. MEMBERS: Agreed.

Honourable J. WALDO MONTEITH (*Minister of National Health and Welfare*): Mr. Chairman, I wonder whether, this being the first meeting of the committee, it would be in order for me to introduce some of the officials of my department who are here with me?

The CHAIRMAN: Yes, sir.

Mr. MONTEITH: Mr. Chairman, on my right is Dr. G. D. W. Cameron, deputy minister of national health and welfare, and then Dr. C. A. Morrell, chief of the food and drug directorate; Mr. R. E. Curran, the department's legal advisor and Mr. Eric Preston, chief of personnel services.

In addition to the director, the following senior staff members from the department of food and drugs are present:

Dr. L. I. Pugsley, associate director; Dr. R. A. Chapman, assistant director in charge of scientific services; Dr. J. B. Murphy, chief medical officer; Mr. M. G. Allmark, chief of the pharmacology and toxicology section; Mr. Paul Soucy, chief of the proprietary or patent medicines section and Mr. R. C. Hammond, chief of the narcotic control division.

I think generally these will be the chief people of the department who will be available to supply information to us.

You will all have read many press reports, and heard a great deal said in the commons chamber, on the death-dealing properties of certain drugs, and on the general pollution of his environment by man himself.

In this committee, which certainly has an immense task before it, you will have an opportunity to learn at first hand of the views of the experts in medical and scientific fields. You will, we trust, utimately be able to put this whole picture into perspective, in your own minds and in the minds of all Canadians.

The apparent effects of thalidomide will be with us through the lives of every man in this room, as its victims grow into the world.

It is our job to ensure that these victims are cared for in the best possible manner, that their needs are met to the fullest extent we can devise, and to ensure, as much as is possible, that a similar tragedy will never occur again.

But we must also bear in mind that thalidomide is still a good drug. It was its side effects, as later evidence indicated, that can be harmful. It induced sleep quickly and without ill effect, but we have learned that it should never be taken during pregnancy.

I am not standing in defence of thalidomide, but it must be pointed out that even the common headache remedy can be dangerous, and cause death, if misused.

There is no such thing as a completely safe drug. The safety factor must be weighed against the value of the drug in relation to its own known dangers.

Penicillin is an example. It has saved millions of lives. But some people, sensitive to it, have died. Should we prevent the sale in Canada of penicillin?

Canadians must be allowed to enjoy all the benefits of scientific discovery—and there have been many in recent years—but they must also be protected.

When the risks cannot be avoided, they must be reduced as much as possible to the point where the balance will be on the side of promoting health and not compounding suffering.

This committee was set up by the government with a twofold terms of reference. It is being asked to consider and report upon:

(*a*) The law and practices relating to the control of the introduction, marketing and use of drugs;

(*b*) The dangers arising from the contamination of food by the use of cemicals to kill weeds, insects and other pests.

I understand from the chairman that the committee will attempt to concentrate first on the drug question and I, too, will do so today.

I will, of course, follow proceedings with intense interest. I would be pleased to return at a later date to explain fully the department's role in the protection of Canadians from chemical contamination.

Both questions deserve undivided attention and I commend the committee for separating one from the other as much as possible.

The responsibility that every Canadian receive the utmost protection in the use of drugs is one that cannot be discharged by any one division of government. The burden must be shared by manufacturers of drugs, the medical profession, pharmacists and even individual Canadians.

The role of the government is not to delay or deny the benefits of science to Canadians, but to ensure that drugs reach the market only after all reasonable precautions have been taken to inform the medical profession of any risks and of any undesirable side effects.

Increased drug safety is a goal we are always striving for.

Our objective was increased safety for the public when we introduced in Parliament last October legislation reinforcing aspects of our drug control provisions.

The changes in our Food and Drugs Act provided authority to impose additional controls on the distribution of drug samples; authorized the prohibition of the sale of a drug, and emphasized that new drugs require special consideration.

Our aim is also safety when we require that a manufacturer take every precaution possible in introducing a new drug.

There must be quality control, exhaustive animal and clinical testing and the provision of detailed information to the medical profession.

It is also the responsibility of government to maintain a staff competent to administer the food and drug legislation.

The job of this staff is to provide adequate technical advice, conduct analyses and tests of drugs, do research and carry out field inspections.

Members of this committee will recall that the staff question was one of the principal points raised in the report of the special committee on new drugs of the Royal College of Physicians and Surgeons, which I tabled in the house last week.

I hope this committee will examine its report most exhaustively, as I consider that the findings and recommendations are of the greatest value.

Dr. Brien, the committee chairman, will be available for any enquiries you may wish to direct to him, and I am sure that his research into the systems employed by governments other than our own could also be of benefit to you.

Dr. Brien's committee felt that the staff of the food and drug directorate was not as large as it should be.

We are aware of this and have for some time been trying, with some success, to increase staff there.

Its director, Dr. C. A. Morrell, is here today to appear before the committee and will be available to answer questions in an effort to give you a complete picture of the directorate's operations.

There have been suggestions—and there will probably be more—that the directorate increase its staff to the point where it can conduct original research into all drugs introduced in Canada.

Some seem to think that too much onus is placed on the companies and not enough collaborating research is performed by the policing agency.

Our firm conviction is that we must insist a manufacturer accept full responsibility for something he puts his name on and sells to the general public.

Any softening of this conviction could result in the weakening of one of the principal elements of our control program for the protection of the public.

This does not mean our responsibility is lessened or that we are relying on the companies to do everything.

Our job is to see—to insist—that the companies do their job and, from time to time, to check on their work, and to carry on sufficient research and investigation in our own establishment to be able to not only check the work of the manufacturer, but to form well-based opinion on the quality of the work being done with a special eye open to possible dangers to the consumer.

Under the present system, manufacturers are required to submit detailed reports on the development and testing of drugs—tracing this process through laboratory and clinical stages. Our experts can—and do—detect shortcomings by scruitinizing these reports. They then require supplementary information.

To have our people retrace the experiments already conducted by the manufacturers would appear to be cumbersome and unnecessary. It would mean a gigantic staff, needless repetition, huge cost, and, in effect, might lead to eventual subsidization of the industry.

I don't think we could justify this to the taxpayer.

The present system has worked well. Our Food and Drugs Act is second to none in the world. It has been used as a model by the World Health Organization.

It sometimes takes years for drugs to win approval of the food and drug experts—some never do. Companies are repeatedly asked for additional information.

In the last 11 years, the directorate has passed some 2,000 new drugs through its screening process with results that were not questioned until very recently.

In other words, every possible care now is taken to ensure that Canadians are protected. And the system now used appears to be working.

But there can be improvements in any undertaking. We are looking to this special committee to make valuable suggestions for such improvements.

This is why the government called the committee. It will hear evidence from experts in many spheres and their advice will be of great help in formulating future government policy.

The thalidomide tragedy has spurred us all to greater action. The government, as you know, not only introduced new legislation, but also made plans for strengthening the food and drug directorate.

Last August, I announced to the provinces that the government stood ready to share the cost of rehabilitation of thalidomide victims. Since then, a number of fact-finding groups have been working to add to federal and provincial knowledge of the problems in this sphere. The expert committee on habilitation reported last week, and copies were tabled in the house.

There is one point that should be stressed—the problem of drug controls, and the constant exchange of technical information that is needed to make such controls completely effective, is not Canada's alone. Nations in many parts of the world have turned their attention to it in recent months.

Before the thalidomide stories had gained prominence in our newspapers, the Canadian Government took action that could have far-reaching results.

It initiated and co-sponsored a special resolution on drugs at the World Health General Assembly in Geneva.

It is hoped that the resolution will lead to an improvement in the exchange of drug information among nations of the world, and further the standardization of procedures regarding new drugs.

Prompt, world-wide exchange of information of new drug developments would help to a great degree in preventing the recurrence of a thalidomide tragedy.

In this opening statement I would like to wish members of this committee every success in their deliberations. They have taken on an onerous task, the completion of which should result in great benefit to all Canadians.

Mr. Chairman and gentlemen, I might just add that naturally I will be available and will be at the committee's beck and call at any time it might wish to have me before it. It does happen that other meetings are frequently held on Tuesdays and Thursdays, and at certain times perhaps I could be excused from this committee's meetings although I will always be available for questioning. I am wondering whether this will be satisfactory, and I make this request so that you will appreciate why I perhaps am not present at every meeting of this special committee.

The CHAIRMAN: I would think that would be satisfactory. It this agreeable to the committee?

Some Hon. MEMBERS: Agreed.

The CHAIRMAN: Gentlemen, has anyone any questions to ask?

Mr. ORLIKOW: Mr. Chairman, I should like to ask the minister several questions. First of all, I have had some correspondence with people in the field such as doctors, who are still concerned as to whether the department actually has the authority to order the withdrawal temporarily or permanently of a drug which has been approved, but in respect of which in latter stages there may be new evidence indicating there are difficulties. It has been said again and again by people in the field that this was a primary difficulty in respect of thalidomide, and that after some information was available which should have indicated that at least the use of the drug should be temporarily suspended, it was not because the department had to work more or less by voluntary cooperation and that the department therefore waited because of certain uncertainties. Certainly we would all hope that there would not be a recurrence of what happened with this drug, but if there were another incident like this, does the law, as it is now written, give the department the authority to order a drug company to halt the distribution and to withdraw immediately all the drugs which have been investigated?

Mr. MONTEITH: Yes, we believe it does; by putting the drug under schedule H we prohibit the distribution, the sale, and so on of a drug. We can do this by order in council.

Mr. ORLIKOW: I think this is pretty satisfactory.

I would like to ask Mr. Monteith another question. On December 28, 1960, Dr. Morrell issued a trade information letter No. 191 which went out to a large number of people. I will read the memorandum.

> In the interests of public health it is now considered necessary to stengthen the regulations under the Food and Drugs Act in respect to the conditions under which drugs are manufactured for sale in Canada. For this purpose I propose to submit the attached regulations.
>
> The Honourable, the Minister of National Health and Welfare.
>
> I will be pleased to have your comments and suggestions on or before March 31, 1961.

One of the points which was included, and I quote, is (i):

> A system of control that will permit a complete and rapid recall of any lot or batch of a drug from the market when such is found to be unsatisfactory or dangerous.

I understand that those recommendations were never implemented. I wonder why they were not because it seems to me that that one in particular would have given the department all the authority necessary to handle the thalidomide problem. According to the information I have it was never implemented.

Mr. MONTEITH: I may stand corrected on this but my understanding is that these regulations, and any set of regulations which we bring out as indicated by that letter, are taken up with various groups in an effort to have the most satisfactory and worth while set of regulations possible.

Dr. Morrell, am I right in saying that some of these regulations are still being considered?

Dr. C. A. MORRELL (*Chief of Food and Drug Directorate*): Yes, Mr. Monteith, they are. I might say that if Mr. Orlikow reads the rest of it he will see that those records must be kept by the manufacturer, and certainly such was the case at that time; I think it was in 1960.

Mr. ORLIKOW: Yes, December 1960.

Dr. MORRELL: We certainly had the idea the manufacturer himself would do the recalling but he must keep records so that he would know how to do this in a most efficient and expeditious manner. It was our hope to have it required by law to keep such records so that the manufacturer himself could recall a remedy if necessary.

Mr. ORLIKOW: But in any case it was not done, Mr. Chairman. This is the point I am making. After Dr. Morrell has spoken I would like to ask him some questions about the whole matter, but it does seem to me, and it was brought to my attention by people in the field who expressed their opinion in a letter to me, that these regulations being put into effect would have given the department the authority needed to move much faster in the thalidomide problem. I am just curious about why there was objection from the manufacturers and difficulties which were not foreseen when Dr. Morrell sent out these proposals.

Mr. MONTEITH: Mr. Orlikow, I think we can answer your question better by questioning Dr. Morrell, and subsequently I would be pleased to speak on it.

Mr. ORLIKOW: The only reason I raise this, Mr. Monteith, is that I would like to know whether Dr. Morrell recommended it and you countermanded it.

Mr. MONTEITH: I do not recall the details of it, but I would like to hear Dr. Morrell give his side of the story.

The CHAIRMAN: To save any duplication, can we have Dr. Morrell of the drug directorate make his statement and make us aware of his views, and then both the minister and the director would be prepared to answer questions simultaneously?

Mr. ORLIKOW: I have just one other question to put to Mr. Monteith. The report which was tabled from this special committee made some pretty specific recommendations about increased staff for the department. Mr. Monteith said in his opening statement that the department was giving it favourable consideration. I forget the exact words he used. I wonder if you have accepted pretty well the precise recommendations they made and if you have accepted their recommendations as to how many more people you need. I would also like to know if you have some idea of the time it is going to take, a year or two or how long, until you get that extra number of people which they recommend.

Mr. MONTEITH: Actually the increased staff which has been requested for some little time has been the following. This was before the report came in and before we knew what the report was going to contain. We had then requested certain increases and approved increases prior to the report. In the new drug submission field they are the following: One medical officer, one technical officer, two support staff, two chemists. This is in the pharmacology and toxicology division, two chemists and one support staff. Pharmaceutical division, one chemist and one support staff; microbiology, one bacteriologist and two support staff.

Now, this has been recommended and accepted at the moment, but, as I said before, the actual report was received and the staff will again be looked over with a view to the suggestions in the report.

Mr. ORLIKOW: Those are your recommendations as far as the staff complement is concerned. Is that as far as your establishment is concerned?

Mr. MONTEITH: Yes, the increase in the staff.

Mr. ORLIKOW: But they have not yet been hired?

Dr. MORRELL: They have hired one man, but recruiting is a difficult problem I might say.

Mr. HAIDASZ: Why does Dr. Morrell think that recruiting is so difficult? Is it because of the wage scale or because of a lack of men qualified to fill the jobs in Canada?

Mr. MONTEITH: I still think this is a question which Dr. Morrell can answer much more readily and exactly than I can.

Mr. MARTIN: I would like to ask a question. Mr. Orlikow asked a question which may have left a wrong impression. He asked the minister if he had countermanded any suggestions made by the director. The minister then replied to that "I think we had better wait until Dr. Morrell gets on the stand." I am sure the minister did not mean to leave that impression.

Mr. MONTEITH: I certainly did not mean to leave the impression that I countermanded any suggestions made by Dr. Morrell, but I still feel the whole question could probably be better taken up by him.

Mr. MARTIN: Did you countermand any suggestions made by Dr. Morrell?

Mr. MONTEITH: Not to my recollection.

The CHAIRMAN: I think I interrupted the minister at that stage and asked the committee if Dr. Morrell could make his statement so that we could have both statements before us. Is that in accordance with the wish of the committee?

Mr. MARTIN: You did, but I thought that was the wrong procedure in view of the impression that Mr. Orlikow had left. Now, the minister has said that to the best of his knowledge he did not countermand any suggestion made by Dr. Morrell.

Mr. ORLIKOW: I did not make that suggestion. I just thought this should be in the record of the future. I have no knowledge and I made no suggestion at all that the minister countermanded any recommendations made by Dr. Morrell.

The CHAIRMAN: Could we now have Dr. Morrell's statement? It is agreed.

Dr. MORRELL: Mr. Chairman, I have prepared a statement on the procedures used by the food and drug directorate in handling new drug submissions. I think this has been distributed to each member. It may be rather dull reading but I am prepared to read it.

The CHAIRMAN: I think we should have it read.

Dr. MORRELL: Although the regulations imply that the new drug submissions should be sent to the minister, they are usually addressed to the director. If they are sent to the minister, they are sent from there to the director's office. The director's secretary sends them at once to the medical section.

In the medical section they are examined, first of all, to determine whether or not the drug in question is a new drug as defined by section C.01.301. In the great majority of cases the drug is found to be a new drug. In either case the manufacturer is notified of the receipt of the submission (usually on the same day) and if it is a new drug, pertinent information relating to it is entered on a file card and in a ledger. There are some cases where it takes a good deal longer to make a decision, but usually on the same day the manufacturer gets a receipt of the submission.

Mr. NICHOLSON: Most of us know what a drug submission is but it would facilitate matters if Dr. Morrell could explain what it is at this point.

Dr. MORRELL: I am afraid it is going to be dull. Section C.01.302 of the present regulations requires every manufacturer to submit to the minister what we call a new drug submission in respect of any drug that is new as defined in the regulations. There is a definition of the new drug in the regulations.

In the present regulations, section C.01.301, this definition appears. This submission has to be made in the form, manner and contents satisfactory to the minister. It should include all the information that the manufacturer has in respect of that drug. It should include the chemical structure, composition; the methods of control; the methods of manufacture; the labelling; the claim the manufacturer is going to make; the pharmacology and toxicology of the drug; the clinical results of the tests to discover what hazards are encountered in the use of the drug; the dosage in which the drug should be given in the usual course of treatment; the pharmaceutical form in which the drug is put up for use, and so on. All of this infromation on these subjects must be included in the new drug submission. It is then required that this information be filed in duplicate with the minister before the drug is put on the market in the usual commercial way. Prior to this, of course, the manufacturer must have used the drug both in the laboratory and in the clinic in order to collect the information.

Provision is now made under section C.01.307 of the regulations to allow him to do this. He must, before sending out a new drug for clinical trial, notify the minister that he is going to do so, supply the minister with a name or a distinguishing mark by which the drug is known, he must label it—there is a special statement required on the label which says "for use by qualified investigators only"—and he must send it only to a qualified investigator. He must also keep records of the reports of these investigators on the results of that clinical

trial, and if the minister, or the director in this case, requires to see these reports, he must make them available to the director for examination. That is all covered under present section C.01.307.

Mr. NICHOLSON: Thank you.

Mr. VALADE: Can I ask a question in this regard? What is the essential element required to classify a drug as a new drug in comparison with similar drugs that could be on the market?

Dr. MORRELL: There are several reasons for calling a drug a new drug. No. 1, and the one that occurs probably to all of us at once, is that it is a new chemical structure that has not been used previously in medicine. It may have been known but not used for medical purposes, or it may have been developed simply for medical purposes. These things are now appearing on the market because the pharmaceutical industry is interested in developing new products. If it is a new compound obviously it is a new drug. Now, a combination of known drugs that have not been previously used in combination, is also a new drug. It may be a combination of two or more perhaps well known drugs. This is, in most instances, called a new drug. If it is a combination of known vitamins, it is not considered to be a drug. A decision must be made as to whether the combination used is really to be considered as a new drug.

If a known drug has been recommended for a brand new use in medicine it is a new drug. Let us take as an example aspirin which has been known for 60 years or more; let us suppose that someone came out today with a recommendation that aspirin was effective in the treatment of cancer. In this case we would consider that aspirin in that context was a new drug and we would require the manufacturer to submit evidence on the effectiveness and safety of the drug under those conditions of use. If a drug has been given by the oral route, that is taken by mouth, and some manufacturer finds that it would be more effective or beneficial if injected, then we would also consider that to be a new drug. These are the main categories of new drugs and they are defined in the existing section C.01.301. A new drug therefore is not just a new compound, but it also has those connotations.

Mr. VALADE: Let us follow this line of questioning, Dr. Morrell. Did you classify thalidomide as a new drug compared to other brands of tranquilizers with other brand names in America, such as Stemetil?

Dr. MORRELL: We classified thalidomide as a new drug because it was a new chemical structure, so obviously it was a new drug. There was no debate on that with the manufacturer or with anyone else. I continue with my statement.

A clerk then prepares a routine form and the new drug submission is taken to the central registry where it is given a file number. The submission is then put into a docket, together with forms for routing and recording of comments, and sent to the associate director. The duplicate copy of the submission is kept by the medical section.

The associate director examines the submission in reference to the type of drug and the claims made for it and sends it to the appropriate laboratory section.

The laboratory, using criteria related to the recommendations for use of the drug, and those are recommendations given by manufacturers, reviews the pharmacological, toxicological and clinical work and also the chemisty, the manufacturing controls including the method of analysis. An actual trial of the method of analysis is seldom made at this stage.

It should be noted that the submission may be passed to more than one laboratory section; it may go to two or three sections if there is data or information in it requiring expert comment by specialists in different disciplines.

The laboratory people do not make their comments on the form provided but write them as a summary of the data and information given in the submission with comments on their adequacy in relation to the criteria presented in a guide used for this purpose and when they have finished with it, the submission and the comments are returned to the associate director.

The associate director studies the comments made by the laboratory people and checks them with the information given in the submission. He always examines critically the claims and proposed promotional material and frequently discusses with the laboratory people their comments, objections and suggestions on the whole subject matter in the submission. He may also discuss at this point, any questionable features in the submission with the medical section. Finally, the associate director sets down a summary on the form provided, of his own comments, remarks and recommendations in respect to the submission, and returns the submission and the accompanying file of comments to the medical section.

It is the duty of the chief medical officer together with his chemist assistant to then review all the reports and the submission itself. Special attention needs to be paid to the manufacturing controls described and to the clinical data. The nonproprietary (proper) name, if there is one, is recorded or decided upon at this time and in conjunction with the associate director, whether or not the drug should be a prescription drug. If there is any deficiency found in the new drug submission, a letter is written to the manufacturer by the chief medical officer pointing out what is missing or what is wrong with the submission and stating that further information is necessary or that something contained in it is unacceptable. Such a letter to the manufacturer states also that the new drug submission is not acceptable in its present form.

If, however, there is no objection taken up to this point and if everything else is satisfactory, the submission is sent to inspection services for a review of the labels. Labels are examined for compliance with the labelling requirements of the food and drug regulations. Inspection services also review the wording of promotional material and if they find it objectionable the matter is reported to and discussed with, the medical section. Inspection services then return the submission with their comments to the medical section. At this point a new drug card for the product in question is completed and a new drug acceptance form is made out. Very frequently a letter is also written to the manufacturer pointing out some objection to the labelling or other similar matter that must be corrected. Both the new drug acceptance form and this letter are sent to the director who signs them both and they are then mailed to the manufacturer. This is a standard form and the wording is the same for all new drugs.

The Director may be informed, at any time during this whole procedure, that there is some special difficulty arising or that disagreement with the manufacturers has occurred during the processing of the submission. Such information, depending on the seriousness of the difficulty, may lead to a conference of food and drug officers or a conference which includes the manufacturer's representatives as well as food and drug staff, for the purpose of establishing or clarifying a policy or resolving the disagreement in a manner that is proper and in conformity with the requirements of the act and regulations.

In actual practice, the number of conferences on new drugs in which the director is involved is smaller than those in which the associate director, the laboratory staff or the medical section take part. These latter meetings are fairly numerous. There is considerable correspondence and often telephone calls and visits from the manufacturer's medical or technical staff in connection with many new drug submissions.

The regional and district offices are advised by a monthly sheet of the new drug submissions received and of those pending or cleared. They receive as well, a card summarizing the new drug submissions cleared which is intended to be filed under proper (non-proprietary) name, brand name and manufacturer's name.

Processing of Supplementary Information

After a new drug submission has been accepted, any deviation in the use, composition, pharmaceutical forms, etc. from information and data given in the original submission, may be the subject of a supplemental submission. A supplement may involve a change in (1) the trade name, (2) the method of manufacture, (3) the dosage or dosage forms, (4) the method of analysis, (5) the labelling, (6) additional active ingredients, (7) additional inactive ingredients (colour, flavour, excipients, etc.), (8) additional claims. If there is a significant change in the active ingredients, method of manufacture, route of administration or dosage forms so that the safety is questionable, the so-called supplement may be classified as a new drug submission and entered and handled accordingly. If it is a relatively simple change in the formulation, labelling, method of analysis, manufacturing process or a small extension of the claims, it is considered as a supplement and handled as soon as possible. If a reply can reasonably be expected to be given within two weeks, the information is not acknowledged. If it appears that a longer time will be required for review, the receipt of the supplement is acknowledged. Supplements are not numbered but a record is kept of all correspondence in the correspondence record book. If the supplement involves the use of a new trade name, a revised card is issued. If it involves a new dosage unit, a new card is usually issued, but not always.

Since supplements may range all the way from one paragraph in a letter (e.g. notification of change of address or a change in a trade name) to a number of volumes (if they are trying to justify an extension of claims), it has been difficult to work out a standard method of handling them. We have been forced to do the best we could with the staff available.

Mr. NICHOLSON: Mr. Chairman, I would like Dr. Morrell to indicate how many new drug submissions they may have in the course of a month or so?

Dr. MORRELL: I have a table here which indicates the number for the last four or five years. This is a list of bona fide new drug submissions received, not including supplementaries. During 1958 there were 162; during 1959, 197; during 1960, 197; during 1961, 150 and during 1962, 177. Someone has made the addition and it is 883 for those years.

Mr. NICHOLSON: If a drug has been accepted in the United States, Great Britain or some other country of the world, it would still be a new drug submission in Canada, is that right?

Dr. MORRELL: Yes, sir.

Mr. NICHOLSON: Thank you.

Mr. HARLEY: I should like to ask Dr. Morrell whether he would go through the steps that take place before it becomes a new drug submission? In other words, how does the drug company inform you that they are going to put a new drug up for experimental purposes? What is the procedure followed before it reaches this stage?

Dr. MORRELL: Mr. Chairman, they notify us by a letter that usually gives some information. If I may say so, at this stage, and perhaps it is a little early, I think we need some strengthening of section C.01.307, which is the section I am referring to and which covers the restrictions on the

distribution of what we now call drugs for investigational use only. The manufacturer informs the minister of an identifying name or mark by which the drug can be recognized. That is the first thing, and that has a practical value from an enforcement standpoint. If this drug comes into the country from outside, and I can tell you that a great majority of them do, at least we can notify our inspectors at the customs that such and such a drug with the mark of such and such a kind is to be admitted if it is addressed to the proper people.

It should be labelled also, of course, "to be used by qualified investigators only."

The manufacturer prior to making the shipment must assure that any person to whom the drug is sent is a qualified investigator and has the facilities for the investigation to be conducted by him. This individual must assure the manufacturer that the drug will be solely used by him or under his direction for investigation. That information must be obtained by the manufacturer and that assurance given to him in writing so that we can see that he has received it. The manufacturer as well must keep accurate records of such distribution and the results of such investigation and make these records available for inspection by the directorate.

Those are the total regulations in force now at this moment covering drugs for investigational use prior to the submission of a new drug submitted to the minister.

Mr. HARLEY: I was wondering in respect of the qualifications of researchers whether this is something to be considered by the manufacturer and in respect of which the department has nothing to do at this stage?

Dr. MORRELL: We can argue about that, sir, but as far as the final decision is concerned, it would have to be made in court. If a manufacturer refused to accept our arguments and wished to carry on, it would be up to the magistrate or the judge to decide whether the persons to whom the manufacturer had sent the drug were really qualified investigators.

The CHAIRMAN: Dr. Morrell, have you the power under the act to initiate such action?

Dr. MORRELL: We can always initiate action for a violation of the regulations. This would in our opinion be a violation of the regulations, that is, if we disagreed with the qualifications of the investigator.

Mr. BALDWIN: Dr. Morrell, I wonder whether you would speak a little louder when you are carrying on a discussion with someone closer to you?

Dr. MORRELL: Yes. I am sorry.

Mr. VALADE: Dr. Morrell, I should like to ask you a question. When you have cause to think that a drug should be investigated further, do you advise the pharmaceutical or medical organizations in each province, or what is the procedure taken in this regard?

Dr. MORRELL: Are you referring now to a drug that is in the category of a drug for investigational use prior to marketing?

Mr. VALADE: Yes, I am referring to drugs in this category prior to marketing.

Dr. MORRELL: No. We have had very little experience and very little action in respect of drugs for purely investigational use. They are not yet the subject of new drug submissions and are simply put out for trial to a qualified investigator.

We have had some action and have taken some action in this respect, including one action not too long ago, which you may remember. In that case we notified the manufacturer that he must cease distribution for that purpose or

any other purpose. Our charge would be that he had violated a portion or all of section C.01.307, if it came to a court action. We do not make this information public. Nor do we notify anyone else as a matter of fact and have not up until the present.

Mr. VALADE: Is that true even though a new drug has been accepted and it has been discovered that there are some secondary effects which have been drawn to the attention of the directorate, or do you then advise the medical or pharmaceutical bodies in this nation?

Dr. MORRELL: No, and it is quite common, as you may know. A drug is in the market for some time with wide use on a large number of patients—it may have been millions, and by a great number of medical practitioners, many thousands—and you will discover, or someone will discover a side reaction or a contra-indication which was not revealed when the new drug submission was made. Our law requires the manufacturer to give adequate direction for use. Also the act itself in section 9(1) prohibits anyone from labelling, advertising or promoting a drug in a matter that is false, misleading or deceptive or likely to give an erroneous impression regarding its safety.

So, falling back on this law and this authority, we have required all manufacturers to give adequate directions for the use of their products, and the term "adequate directions" would certainly require them to give warnings of side effects or contra-indications. The law makes this the responsibility of the manufacturer. Our responsibility is to see that he does do so. So that the manufacturer then sends out a warning, or puts it in a package circular his directions for the use and a notation of any new contra-indication or new undesirable side effect so that the doctor himself can be aware of all of the dangers that are known about the drug at any given time.

Mr. VALADE: I should like to follow up this discussion with one further question, Dr. Morrell. Have you in the past communicated by letter or advised those medical or pharmaceutical bodies or organizations representing these medical professions of any of the new developments in regard to drugs?

Dr. MORRELL: We do communicate with the pharmacists and the doctors in respect of drugs. One of the most common bits of information we give them is information about a drug put in the "prescription only sale" category. It is, of course, essential for these people to know and we issue an annual card which is sent to I think every practicing doctor and every practicing pharmacist in the country to inform them as to what drugs now may be sold retail only on doctor's order. This I think is the main communication we have had with the medical profession as a whole in the past.

In recent months we have, of course, sent several letters—I think three, but two anyway—directed to individual doctors, or at least to the medical profession, in respect of thalidomide, in one case, and other drugs in respect of which we had some information regarding possible certain associated side effects that were undesirable. We have informed them of these things.

This is a new policy in so far as the administration of the act has been concerned. We have always, up to this year at least, considered that it was the manufacturers' responsibility to inform the profession or the public, and in the case of the public, to warn on the label of any reasons for dangers in respect of the use of a drug.

Mr. ORLIKOW: Mr. Chairman, I should like to ask one question, without being critical, in respect of the thalidomide incident. Having regard to the system of holding the manufacturing company responsible for doing the investigation work in regard to drugs and in the light of what happened with the use of thalidomide, is a new policy necessary, and if so what does the department think should be adopted in this field? I raise this question because I know

that my wife had taken thalidomide over a period of time before the adverse information was available, and although it did not create difficulties in the usual sense there certainly was some kind of an effect—I will not use the term "breakdown" because I do not wish to exaggerate the situation. There was also quite a substantial lapse in time in the information getting from the companies to the doctors and then to the patients. I am aware of many cases in which this did happen and I am wondering whether, in the light of the fact that we are using so many more new and very potent drugs, a review of the procedure of leaving this up to the manufacturers is not necessary. After all, the manufacturer, and I am not being critical at the moment, is interested in selling his drugs and may not be in such a hurry, as would the department, in transmitting this information. I am wondering whether the policy followed now is sufficient unto itself, particularly in light of recent developments.

Dr. MORRELL: Mr. Chairman, certainly in the light of hindsight I may say that it probably is not sufficient. I think we are going to ask the minister for authority in the regulations to remove certain investigational drugs, or new drugs from the market and return them, at least to the new drug status, when sufficient evidence is available to indicate that something should be done.

In respect of the thalidomide incident, and in light of the knowledge we had at that time, and the information that was supplied to us,—I think you all have copies of the yellow book in respect of the information that was given to us—I feel that there was no delay in taking the action that was provided for in the Food and Drugs Act and regulations.

The CHAIRMAN: Excuse me, may I interrupt you for just a moment? This yellow book can be obtained on request. This is the information with regard to the thalidomide drug and is printed in two volumes.

Dr. MORRELL: The manufacturers met with our group on December 1 and gave us very sketchy information as to what they had heard was happening in Europe. Our reaction was to require them to give doctors this information at once. On December 5, one company sent out a letter and on December 7, the other company sent out a letter to all medical practitioners in Canada warning them that thalidomide was not to be used, because it was contra-indicated, in other words, in women of child bearing age. I think on looking back on what I know, that warning was very effective, Mr. Orlikow, but certainly hindsight is better than foresight.

We feel that some authority should be provided to require that a manufacturer recall a drug at once whenever the minister feels that there is sufficient evidence criminating a drug, until the matter is cleared up.

I know that Dr. Brien's committee has also suggested that we be given authority to do this.

Mr. VALADE: Dr. Morrell, you just mentioned the term "sufficient evidence" in respect of certain drugs. Is that not a term which involves an awful lot of discussion?

Dr. MORRELL: And how!

Mr. VALADE: I think one of the difficulties arises in regard to a decision as to what is sufficient evidence and what is not sufficient evidence.

Dr. MORRELL: I do not think you can regulate in this regard, sir. I think this has to be a matter of judgment which leans far backward.

Mr. ORLIKOW: If this involves a matter of judgment in your department, then it becomes a very simple thing because then, depending upon what happens, the public will be able to decide whether the judgment exercised was proper or not. If this involves a matter of judgment diffused between your department and the manufacturing companies, as seems to have been the case

in the past, then how can anyone establish if a mistake has been made, when it was made, where it was made and by whom it was made? It seems to me this is an important matter, Mr. Chairman. I raise this matter in respect of thalidomide not because of what has happened but because I feel that we should surely learn some lesson for the future.

The CHAIRMAN: I think that is precisely the reason this committee was set up.

Mr. ORLIKOW: Therefore, Mr. Chairman, has it not been established sufficiently that judgment must be vested with the department? This does not mean that there may never be medical action, at least from a local point of view, but I think we have to be sure that the department has to widely use its judgment when dealing with these requirements.

Mr. NICHOLSON: It is my understanding, Mr. Chairman, that that is a recommendation of the special committee.

The CHAIRMAN: That is right.

Mr. HARLEY: Mr. Chairman, I should like to ask a few questions in regard to control in Canada. We are concerned with safety, and it certainly does influence the workings of the department. Do drug or manufacturing companies have to prove or satisfy themselves not only as to the safety of a drug, but as to its effectiveness in respect of the reason it is prescribed?

Dr. MORRELL: Dr. Harley and Mr. Chairman, safety is, as you know, a very relative term. First of all, I do not think the manufacturers can prove a drug to be safe in the popular usage of that term. Safety is a relative term. In respect of drugs it is never absolute, and to ask a manufacturer to prove that his drug is safe I think would finally lead to the rejection of most drugs. So that we really look for information as to any possible hazard or danger and the evidence of such which turns up in the clinical trials and investigations of the drug during the investigational period. This is the thing we really look for primarily.

You cannot help but look for evidence also of effectiveness. I think this goes along with your scrutiny of a new drug submission in respect of so-called safety. We have been in the habit, of course, of looking for the effectiveness or evidence of effectiveness which is claimed for it by the manufacturer, or will be claimed for it when it is on the market. We have at times questioned the evidence that is supplied in this respect but it has not been a prime consideration. The prime consideration has been to get evidence as to the proper dosage, proper use, and hazards that accompany its proper use as well as the warnings and information that should go to the doctor in respect of the proper use of the drug. The doctor who is going to administer the drug cannot do so unless he knows when he should not give it and what to expect when he does give it. This is what we are really looking for. We do not ask the manufacturer to prove that his drug is effective, if you mean by "prove" that there is no doubt about it.

I have thought about this often enough. If it is effective in 20 per cent of the people you give it to, is that proof, and if it fails in the other 80 per cent of a certain group, in respect of some types of diseases, this would be a welcome addition, I think you would agree. So that we have got away from refusing to admit a drug altogether on the basis of effectiveness.

I note that the Brien committee has made the recommendation that we should require in our regulations "substantial evidence" rather than proof of the effectiveness of a drug.

Mr. HARLEY: Mr. Chairman, I should like to ask one follow-up question. Perhaps this should be answered by individuals of your staff who review these

submissions, but I was wondering whether in the study there is a placebo test, so that some idea can be gained as to whether the drug is effective or not?

Dr. MORRELL: I am afraid they do not, Doctor Harley, but if you wish details in this regard you will have to ask some of the individuals who do the reviews themselves.

The CHAIRMAN: Would you like to reserve that question until we have individuals familiar with this situation before us?

Dr. MORRELL: Doctor Pugsley and Doctor Murphy are both here, Mr. Chairman.

Mr. HARLEY: Mr. Chairman, perhaps it would be of information to some members of this committee if I explained that "placebo" means the use of a substance of no chemical action at all, involving the use of a capsule or tablet containing sugar instead of a drug in order to see if there is any reaction to it.

The CHAIRMAN: Would you like to ask any question in that regard?

Dr. MORRELL: The answer to your question is, not always.

Mr. HORNER (*Jasper-Edson*): Mr. Chairman, I should like to ask Dr. Morrell whether or not teratogenic studies are required in respect of new drug submissions particularly where the new drugs are associated with women of child bearing ages?

Dr. MORRELL: Teratogenic studies were not required prior to the development of thalidomide.

Mr. HORNER (*Jasper-Edson*): Are they required now?

Dr. MORRELL: Yes, not by regulation but by administration.

Mr. HORNER (*Jasper-Edson*): I should like to ask a supplementary question. Is there a reasonably good study in this regard which can be standardized?

Dr. MORRELL: The answer is no. I do not think that you can predict from animal tests what will happen in humans. It is true that several groups of people have been able to produce malformed rabbits in litters, the mothers of which have had thalidomide in high doses, but this has not been uniformally obtained. Other people have been unsuccessful. Several at least have been successful in this regard.

One of our projects, and I am sure a project that is being studied by a great many people not only in industry but in universities, is aimed at defining some reliable teratogenic tests which can be done on animals, embryos or tissues.

Mr. HORNER (*Jasper-Edson*): I have just one further simple question. Do manufacturing firms having large submissions of new drugs have to pay a substantial fee for these processes?

Dr. MORRELL: No, sir, they pay nothing.

Mr. BALDWIN: Mr. Chairman, I was interested in that exchange between Doctor Morrell, Doctor Orlikow and Mr. Valade. In this respect I should like to point out that I have noted from reading the regulations that regulation C.01.303 provides that no person shall sell a new drug where certain material changes are made in the conditions of use, labelling, pharmaceutical form, dosage, strength, quality or purity for manufacturing methods or facilities for control, and I wondered whether we could achieve the purpose behind this discussion by adding thereto, that if it becomes apparent to the manufacturer, or if he discovers that there are side effects or contra-indications, that did not appear in the new drug submission or in the original investigation, that he

shall automatically be prohibited from selling it. Would that be a fair and practical way of solving this problem?

Dr. MORRELL: Do you mean automatically prohibiting it forever?

Mr. BALDWIN: Oh, no, I imagine this would be subject to the regulations, and I am sure that any schedule added to the legislation must be flexible. I am just suggesting that possibly it should be required of a manufacturer which becomes aware of side effects or contra-indications to cease selling the drug because of an automatic prohibition under section C.01.303, perhaps until further direction from the department.

Dr. MORRELL: That would be possible, I am sure.

Mr. BALDWIN: I wanted to go a step further. Do you think it would be fair and practical to do so?

Dr. MORRELL: We have always considered, and I know that this is past history, perhaps, although there has been some good basis for it, that a doctor should be allowed to use a drug providing he is told of all the dangers. He knows then how to use it. As soon as a new side effect it discovered, if he is informed at once, and I mean within a week at the most, then the doctor can continue to use it.

You know that thalidomide is not the only drug that has had a series of side effects. Many well known useful and powerful drugs have been on the market, some of them for four or five years, before it was found that there are certain conditions, or certain groups of people to whom you should not give these drugs because it is dangerous to them and may kill them and, in fact, it has killed some people. As soon as this is known, or we are made aware of this, the manufacturer is required to make this information available at once to all people who are using the drug.

If it is a drug on prescription the only people who are using it legally, at least, are those people who are using it under a doctor's order. We feel that it is up to the medical profession to make their own decisions. There may be conditions in which they have to weigh the evidence. They perhaps must ask themselves: If I do not give it to the man he is going to die anyway but if I do give it there is this danger; which should I do under the circumstances? This is up to the practitioner, I think.

I suppose we could adopt a certain regulation such as you have suggested, but I do not know just how it would work. I am trying to visualize a case in which it would so work.

Mr. BALDWIN: I was not thinking so much of the medical profession. My mind was directed particularly toward the results of your discussions with the manufacturing or pharmaceutical houses which become aware of some side effects or contra-indications so that the prohibition to sell would become automatically applicable to the manufacturer.

Dr. MORRELL: It might be useful if the prohibition were to the effect that he should not sell it until he gave this information to the public and the medical profession. There might be some value in it in that way.

Mr. NICHOLSON: Doctor Morrell, did I understand you correctly to say that on December 5 and again on December 7 a notice went out to all medical practitioners in Canada in respect of thalidomide?

Dr. MORRELL: Yes. There were two companies involved, as you know.

Mr. NICHOLSON: Yes.

Dr. MORRELL: One company got their letter out on December 5 and the other company got a very similar letter out on December 7, addressed to all practitioners in Canada.

Mr. NICHOLSON: Did you see the letters in these cases?

Dr. MORRELL: I saw copies of them, yes.

Mr. NICHOLSON: Were they sent in such a form that the doctor could not help but have his attention directed to the importance of the situation?

Dr. MORRELL: I thought they were sent in a proper manner. They were sent in a long envelope, and it is true that the manufacturers' name I think was on the corner, but also in large bold faced type at the lower left hand corner was printed: "IMPORTANT DRUG WARNING". This was to call to their attention not to throw it unto the waste paper basket.

Mr. HARLEY: Apropos of that I can give Mr. Nicholson copies of it.

Mr. FAIRWEATHER: I would like copies of all of them.

Mr. VALADE: I have a question on administration. Dr. Morrell, how many persons do you have that are responsible to you in the directorate?

Dr. MORRELL: In the whole directorate? They are not all concerned with drugs.

Mr. VALADE: I mean just those concerned with drugs.

Dr. MORRELL: About 40 per cent of our staff works on drugs, and 40 per cent of 400 would be around 160.

Mr. VALADE: Did you make an estimate as to the required minimum number of persons that your directorate would need in order to comply with the necessities?

Dr. MORRELL: It would be difficult to say.

Mr. VALADE: Let us say the minimum necessities.

Dr. MORRELL: I was told a while ago, and I think it made pretty good sense, that if you ask the chief of police how many policemen he needs, he always needs more, but if you ask the mayor, he or she may not be in agreement with it.

Mr. HAIDASZ: I would like to ask Dr. Morrell a question. In view of his experience with this drug thalidomide, what, in his opinion, should some of the new regulations in the Food and Drugs Act be and which of them should be legislated?

Dr. MORRELL: If we start at the beginning, there should be some changes in C.01.307 which is the section related to the control and investigation of drugs. I think we should have authority to demand all information that the manufacturer has at that time. In many cases he has more information than he gives to us. I think the regulation says that all he needs to do is to give us an identifying name in respect to the drug. However, I think we ought to have the authority to say that this is not enough and that we want to know the exact composition. If the manufacturer has not got it, then we want to know something about the nature of the drug, for example, if it is an extract of glands, or else we would like to have the exact chemical composition. He can give us a great deal more information.

Secondly, I think we should have a little closer check on the selection of qualified investigators. It will be difficult I think to define in any regulation what a qualified investigator is because there is such a variety of them that I do not think it would fit a regulation, but something will have to be worked out in this respect to improve what we now have.

Thirdly, I think perhaps we should know in advance to whom the manufacturer is going to send his drug for investigation, whether it be a clinical trial or some other trial. I presume that the minister would have authority to disagree with the manufacturer's proposal if that was thought to be necessary. Certainly, during this stage of investigation the manufacturer himself should have adequate controls to standardize the drug, at least to a certain extent. This is something that we suspect is not always known.

Finally, I think we should have authority to stop a clinical trial promptly at any stage in the investigation if the minister finds that there is some danger to the public resulting from this clinical trial.

The CHAIRMAN: Could I interrupt for one second, Dr. Morrell? Do you have an example where some of these regulations that you would like to have put into effect were not put into effect because of the law? Let us take as an example the Liefcort situation in Montreal with Dr. Liefman. Were you hampered in any way in putting your mechanics into effect because of the regulations?

Dr. MORRELL: I think we were hampered to a certain extent. It revolves largely around what is a qualified investigator. I think we disagreed with Dr. Liefman's definition of the qualified investigator. This was one of the hampering features in dealing with that problem.

Mr. ORLIKOW: Did you have the authority to tell Dr. Liefman, and to make stick, what you considered were qualified investigators, failing which he could not really put his drug on the market?

Dr. MORRELL: Not really, Mr. Orlikow. I know we do not define in the regulations a qualified investigator so it becomes a question for a magistrate to decide. The actual objection we had to the so-called study that Dr. Liefman was undertaking was based on the fact that the reports from the investigators that had been returned to him were unsatisfactory under the terms of section C.01.307.

Mr. HAIDASZ: Mr. Chairman, could Dr. Morrell tell us what is the present status of the drug Liefcort? Has the department recommended to the government to put it on schedule H, or are they still studying this problem?

Dr. MORRELL: The present status of Liefcort is that it may not be used by anybody else but by Dr. Liefman. Dr. Liefman is now a qualified licensed medical practitioner and we feel that we cannot interfere in his practice, but no one else except Dr. Liefman is to use the product. Actually, the product itself labelled as such is not now distributed. He can, of course, prescribe to his own patients any medication or treatment that he sees fit.

Mr. HAIDASZ: I have one more question on the drug Liefcort. Does the director or does the department feel that the drug Liefcort is safe for humans?

Dr. MORRELL: That is a difficult question. Evidence has not been presented that it is. We felt at the time that we were examining the files of Dr. Liefman that there were no reports on the side effects which we would anticipate from our knowledge of the drug at that time. We had to analyse that drug to find out what was in it, and when we knew what was in it we felt that there was not the kind of information we could anticipate, in the report. We have read about the side reactions since, but in so far as we are aware from the information we have we could not say that it was safe or really unsafe. If we took the evidence available to us, it seemed to be safe, but we were still suspicious because of what we considered the inadequate information that was presented.

Mr. PATTERSON: Dr. Morrell, you made reference to the studies that had been carried out by Dr. Liefman in connection with that particular drug. I wonder if there is any significance in the fact that you qualified that reference and said "so-called studies".

Dr. MORRELL: I did not feel that they were proper, thorough and suitable studies to demonstrate what we expected them to demonstrate. I do not think he could have ever submitted a new drug submission that would be acceptable

on the type of results that we saw he was getting from the drug. I also felt that the studies were not thorough or real studies.

Mr. NICHOLSON: Dr. Morrell, in one or two of the regulations, in at least one, C.01.307, the expression "qualified investigator" appears. Now, it is not uncommon in legislation to see a term such as magistrate, or police officer, but when you put an adjective to determine whether a person is qualified or not, you cannot ask a judge to do it. Surely, the use of the term "qualified investigator" implies something when it appears in the regulations.

Dr. MORRELL: It is a good question. It is one that we have often debated: What is a qualified investigator for a particular job? If a drug is reputed to be useful in the treatment of cancer, for example, I think a qualified investigator dealing with the drug would be a man who is specializing perhaps in internal medicine.

He would certainly have to have the services of a pathologist. He would have to know definitely whether the tumour was malignant or whether it was not. In other words, he would have to diagnose whether it was cancer and what type of cancer it was. He would have to be a man with experience and with the facilities to measure any improvement in the condition of the patient. There are many things that be would have to have at his disposal as well as experience and knowledge to be what we would consider a qualified investigator. I would suppose if it was a question of a drug that is going to be recommended for the treatment of, let us say arthritis or rheumatism, the qualified investigator would best be one who is associated with the clinic that makes a specialty of the study of rheumatic diseases and who has all the facilities at his disposal to measure the improvement and to diagnose the illness so as to be sure he is starting out with something that is really rheumatism, to discover, what type of rheumatism, and one who has all the facilities necessary to measure improvement if there is improvement.

Mr. NICHOLSON: In view of what you said, do you not think then the definition of qualified investigator should be written either into the act or into the regulations?

Dr. MORRELL: We are going to try to do it.

Mr. NICHOLSON: Would it not be better to have it written in, in spite of the difficulties?

Dr. MORRELL: But if something came up suddenly that was not there, we would have to run to the minister to get an amendment.

Mr. NICHOLSON: Would you not agree that that would be better than having a general term of this nature?

Dr. MORRELL: It would make it easier to administer.

Mr. ORLIKOW: It seems to me that this is an extremely important point because unless the department has the authority either through the regulations or just through practices, to exert a very large extent of influence, if not control, on what is proper investigation, then it seems to me that the only other alternative, in order to get protection for the public, is to write into the law the actual controls. This is what they seem to be doing in the United States, and many competent doctors feel they are going too far. However, it does seem to me that, difficult as it may be, this is essential. One competent investigator suggested to me that people doing the initial investigation should be full-time people working in a hospital or in a research set-up, and that really part-time people, in the initial stages at least, are not either qualified or not directly enough concerned to do the adequate testing which is required. Yet, he seemed to indicate in his letter that on occasion testing has been done in companies by part-time people who just are not qualified to do the initial testing at least.

The CHAIRMAN: Can I make one suggestion?

Mr. ORLIKOW: I was just going to say, Mr. Chairman, that while I agree with Dr. Morrell and Mr. Nicholson that this may be a difficult objective to reach, it is a must if the department is really going to be able to do the job which is required.

The CHAIRMAN: Before Mr. Harley asks a question, I wonder if Dr. Morrell could relate to us the Liefcort incident? How was it brought to his attention, what happened and what did the department do about it? We might like to have a look at a specific case. Would that be difficult?

Dr. MORRELL: When was it brought to our attention? I am not sure I can tell you right now.

The CHAIRMAN: Perhaps Mr. Harley could ask his question and your assistant can think about it.

Mr. HARLEY: What I wanted to know of Dr. Morrell is whether he could give us some idea at the present time as to how much control work the food and drug directorate actually has. You mentioned that you eventually analyzed Leifcort and found its contents were such and such. I wonder if you could give the committee some actual idea of how much of that type of work you do and how much of it is strictly a quantity measurement rather than a quality measurement.

Dr. MORRELL: Mr. Chairman, the control work we do is certainly not confined to new drugs, and I presume you want me to discuss the whole of it. The number of drugs sold has been estimated from simply counting the number of items advertised or presented for sale in manufacturers' catalogues and distributors' catalogues, so you can see the basis of it. There are about 25,000 or more pharmaceutical products. These are not separate or distinct entities but are pharmaceutical products on the market. The same drug of course may be sold as a tablet, a capsule, in a solution or otherwise, but we would call all of them separate products. I have been told the Canadian pharmaceutical manufacturers association has said that they produce about 75,000 batches a year of all of their products. Then, there are those manufacturers which do not belong to the pharmaceutical manufacturers association, so I am not able to estimate how many batches there would be from them. I would estimate the number is much smaller than the one I have given. As I have said, our function is a police function, and we go to the wholesaler or manufacturer usually, but occasionally to the retail pharmacy and purchase samples of drugs. We bring them back to the laboratory and they are then analyzed. They are analyzed quantitatively.

When we do the testing of narcotics, for example for the R.C.M.P. when they want to know whether it is heroin or another narcotic, we do not have to tell them how much. However, when we analyze a solution or a capsule or a tablet, we would have to know the quantity because it is related to the strength and standard under which the drug is sold. In this case a quantitative analysis is made. There may be several ingredients contained in the drug, so of course a quantitative analysis of all of these ingredients is necessary to know whether the composition at least meets the standard.

Then, there is the second aspect which is required by the regulations: is the drug available to the patient. In other words, if the patient swallows a pill, will it eventually dissolve in his intestines or will it pass right through without solution. There are requirements for the disintegration time of various tablets. A tablet is put through this test to see if it meets the requirements. We do 2,500 to 3,000 analyses of drugs in a year. These of course are aimed at particular areas in which we have reason to be suspicious. They are not just

drawn blindly from any drug on the market because we feel it is necessary to make our efforts tell as much as possible.

Then we do some imports of drugs either in bulk or in finished form, and I cannot give you the number of samples that they take in this area.

Mr. HARLEY: I was just wondering whether you would have a rough idea of how many of those samples were up to standard and how many were sub-standard?

Dr. MORRELL: I think that two or three years ago I did make a study of the number that did not meet the requirements in every respect. Now, I want to make it clear that the requirements are spelled out mathematically. If you have a five grain tablet, let us say, you cannot have less than 95 per cent and more than 105 per cent of the five grains in the tablet. I think in that study, if I remember correctly, very close to 30 per cent did not meet the requirements in every way. A great proportion of these did not meet the requirements in a minor way. In those cases the manufacturer was warned. When it was 80 per cent or 70 per cent or some other lesser or even greater percentage, the product was removed from the market. We feel these to be the most effective means of protection. I think it is also an effective lesson for the manufacturer because he may stand to lose many thousands of dollars in his product.

Mr. RYNARD: Dr. Morrell, I was wondering how many import drugs you hold up and for how long? What would your average be?

Dr. MORRELL: I can get that information for you but I cannot answer it immediately.

Mr. RYNARD: My second question is: how many drugs do you let in on a special permit through the Food and Drugs Act?

Dr. MORRELL: We have no such thing.

Mr. RYNARD: I am going back to the time when there were drugs that were on the market in the United States, for instance, and you could get a special permission to use that drug through the Food and Drugs Act. I am thinking particularly, and you will recall this, of Thiouracil. Quite a long time elapsed here in Canada before it came in. Could you get special permission if you were satisfied that this drug on record in the United States where it was used was a good drug?

Dr. MORRELL: I presume, Dr. Rynard, you got it yourself. If a drug were directed to Dr. Rynard, there was a time when we said: "let it go". If it came to a manufacturer or to a wholesaler, then we stopped it.

Mr. RYNARD: In other words, you did not hold up any clinical work from a medical standpoint?

Mr. ORLIKOW: I would like to get back to this other question which Mr. Nicholson began. Despite the difficulties, what was the thinking of the department on this question of trying to be more specific about what would be considered qualified investigators?

Dr. MORRELL: I think we must do something about it, but I cannot give you a definition.

Mr. ORLIKOW: You are not at that stage yet.

Mr. VALADE: Is it possible to make a schedule that would place qualified investigators in a certain category without being absolute about it? This would define certain basic qualifications in certain fields of medicine.

Dr. MORRELL: Probably. I would think, Mr. Chairman, that we would consult with the Royal College of Physicians and Surgeons or the Canadian

medical association or the society of clinical investigation or some other medical group when we tried to make such a definition.

Mr. FAIRWEATHER: I am interested in what I might call the international warning system. It intrigues me that for instance in many areas of defence we have this system but is there an early warning system in this phase of our life as well?

Dr. MORRELL: There is not yet established an early warning system, but the department of national health representative at the Geneva world health organization meeting last May initiated and co-sponsored a resolution which was adopted I think by the world health organization's general assembly, which asked the world health organization to study this matter with a view to making some recommendation toward setting up such a system. I do not know what action has been taken.

Mr. MONTEITH: Mr. Chairman, is there not supposed to be a report at the next meeting of the W.H.O. in this regard? Perhaps Doctor Cameron could give us this information.

Dr. G. D. W. CAMERON (*Deputy Minister of National Health and Welfare*): Mr. Chairman, that is being considered by the executive board of W.H.O. at the present time. We are a member of the executive board. Doctor Layton is there and this matter is being dealt with.

Mr. HORNER (*Jasper-Edson*): I should like to ask Doctor Morrell as to the present status of LSD. It is, as I understand, included in schedule H, but it is available to qualified investigators, is that right?

Dr. MORRELL: That is essentially correct, yes. In the case of LSD a qualified investigator is restricted in the sense that he must be working in an institution approved by the minister.

Mr. HORNER (*Jasper-Edson*): May I just suggest that we may probably get some policy in regard to a definition of a qualified investigator by questioning some of the individuals who will be coming before us at a later date.

The CHAIRMAN: I hope the committee will keep that thought in mind.

Mr. NICHOLSON: Mr. Chairman, I should like to suggest that perhaps we give those individuals advance notice of our intention to ask for their assistance in this definition rather than taking them by surprise as was Doctor Morrell this morning.

The CHAIRMAN: I might say that anyone who it is proposed to call before this committee will receive copies of the proceedings of this committee so that they will be informed as to what is happening.

Mr. ORLIKOW: Will this be done on a regular basis, Mr. Chairman?

The CHAIRMAN: I am trying to set it up on a regular basis, but I will of necessity require a motion from this committee to print additional copies of its proceedings in view of the fact that we do not now have sufficient numbers to follow such a practice.

Mr. NICHOLSON: Doctor Morrell, during recent months, probably because of the thalidomide and LSD situations, attention has been directed toward the dangers or adverse effect of new drugs. What about the good side effects of new drugs, and I think that as an example we could refer to dramamine; is this left to the individual practitioner to report it to you or to report it to the drug manufacturers? When a drug being used for one purpose is discovered by accident to have good medicinal qualities for some entirely different purpose, how is that information brought to the attention of the professions?

Dr. MORRELL: The clinician who has discovered this new use should report it to the manufacturer, or report it to the medical journal.

Mr. NICHOLSON: Should he not report it to you?

Dr. MORRELL: No, he does not report it to us.

Mr. NICHOLSON: This involves an article in the medical journal or a report to the manufacturer?

Dr. MORRELL: Yes.

Mr. MONTEITH: Mr. Chairman, I should like to correct one statement which may have been somewhat misleading. I think Doctor Morrell mentioned that 30 per cent of drugs were found defective in some minor form or another. Actually this should be 30 per cent of a selected list of drugs in respect of which there was some general thought that something could be wrong, or there was some suspicion about the drug, is that not right?

Dr. MORRELL: Yes.

Mr. MONTEITH: It was not 30 per cent of all drugs that were found to be in this category, but 30 per cent of a selected list in respect of which there was some suspicion.

Dr. MORRELL: I would hope, Mr. Chairman, that I made that clear but apparently I did not. I said that these drugs were selected for particular reasons. We did not take the drugs off the market without having some particular suspicion or some real reason for thinking that enforcement was needed in this area. I pointed out that some of these defects were minor ones, and many were minor ones, so that the impression should not be given that 30 per cent of all drugs in Canada are defective because they are not. These were selected, as I say, with care, in order to make the most use of our man power.

Mr. MONTEITH: It was 30 per cent of that selected group that were found defective in some minor ways?

Dr. MORRELL: Yes.

Mr. HAIDASZ: Mr. Chairman, I should like to direct another question to Doctor Morrell. Leaving the topic of qualified investigators, the next individuals down the line I presume are the distributors. What are the present regulations in force which are imposed on distributors and manufacturers? In other words, do they have to be licensed? Do you have to know who they are, or do they have to obtain a permit from your department? How are they allowed to carry on their business in this country?

Dr. MORRELL: Are you referring to these people in a commercial sense, Doctor Haidasz?

Mr. HAIDASZ: Yes.

Dr. MORRELL: They do not have to notify us in general. They are not licensed in general. Licences are required for certain groups of drugs which are listed in schedules C and D of the Food and Drugs Act. In addition, licences are required for the manufacture, importation and distribution of controlled drugs and by controlled drugs I mean drugs containing amphetamine or barbiturates, which we have in schedule G, some of the hormones, and schedule D which includes injectable antibiotics, vaccines and serums. No one may sell a drug of that type in Canada unless he has been licensed to manufacture them for sale here. This licence is granted under the Food and Drugs Act following an inspection of the manufacturers' premise, a study of the facilities, and when the manufacturer is licensed, the first batch or several batches are released only after repeated tests are carried out in departmental laboratories.

In respect to schedule G drugs, and these were ones that were implicated in the goof-ball sales in the illicit market; since September, 1961, to deal in these, to import or to export, one must have a licence under the Food and Drugs Act.

Then in respect of other types of drugs that are not specifically dealt with under the Food and Drugs Act, but are specifically dealt with under the Narcotic Control Act, all drugs that are listed in the Narcotic Control Act as narcotic drugs, must be sold and handled only after a licence is obtained.

Then there is the Proprietary or Patent Medicine Act which is also administered by the food and drug directorate, and in this case a manufacturer may ask for a registation of his fomula and, if granted, he will be licensed.

Mr. HAIDASZ: Following this question up, Doctor Morrell, could Doctor Liefman be interpreted or recognized as a manufacturer of Liefcort?

Dr. MORRELL: Well, he at one time had a company called the Endocrine Research Laboratories which was for the purpose of manufacturing Liefcort, and I think he was, therefore, a manufacturer of Liefcort.

Mr. HAIDASZ: Did he have a licence from your department?

Dr. MORRELL: No, he had no licence from our department.

Mr. HAIDASZ: Liefcort contains cortisone, does it not?

Dr. MORRELL: It was manufactured as an investigational drug. It was only in the investigational stage, Doctor Haidasz. He had not come to the point where he was manufacturing it commercially.

Mr. ORLIKOW: Mr. Chairman, at the extensive hearings which were held in the United States one of the problems which became obvious was the problem in respect of drug companies naturally being interested in getting their products on the market as quickly as possible. I am wondering whether there ought not to be more control or the right of control by the department enabling it to insist that there be more thorough and detailed clinical trials before the distribution of a drug is allowed, and if Doctor Morrell thinks that necessary, would the regulations have to be changed to give that authority?

Dr. MORRELL: Mr. Chairman, I think that would be a matter of judgment as to whether adequate clinical trials had already been done. I would like to point out in this connecton that most of our new drugs, and perhaps all types, do not originate in Canada but originate abroad or in the United States, and the majority of new drug submissions that we receive contain clinical trials, or the results of clinical trials that were carried out in other countries. This is a matter that was certainly referred to by the committee of the Royal College, and I think recommendations were made by Doctor Brien and his committee in respect of clinical trials which will have to be studied very carefully.

Perhaps I ought to say here that all new drug submissions that come in are not always satisfactory. I would say that more than half of them are sent back with a request for additional information; certainly more than half. I think we have in all at least 52 new drug submissions that have never been accepted, and we have a great many as a matter of fact, in respect of which the acceptance has been delayed for over a year after they were received because we have demanded, (and in this case we can demand) from the manufacturer that he supplement the information he has given us by further clinical testing in certain aspects. A great many of them are held up for this reason for up to a year.

In other words, a manufacturer who sends in a new drug submission will not always—will not often get his new drug submission accepted within a matter of a month or two.

Mr. HARLEY: Doctor Morrell, I should like to change the subject for one moment and go back to an earlier reference to a change in the Food and Drugs Act particularly in respect of controlled drugs such as barbiturates and amphetamines. I think you suggested that this change necessitated a fairly large addition in staff?

Dr. MORRELL: I believe it involved an addition of 21 individuals.

Mr. HARLEY: I wonder whether you could give us some idea of the problem that was prevalent before this legislative change and the effect of this change as it now appears?

Dr. MORRELL: Mr. Hammond is here, who administers this, and perhaps he should answer it. I can give in general terms what I know about it.

Prior to the amendment to the Food and Drugs Act in 1961 and the setting up of schedule G, these drugs were obtained only on prescription as they were already in schedule F, and could legally be bought only on a doctor's order. I presume that the temptation and the demand for them in the illicit market was sufficient to make it profitable and desirable for some people to obtain them in whatever way they could and peddle them on the street corners or in the taverns, or wherever they were sold.

This was a difficult matter for the police to handle because there was no such thing as illegal possession, and if you had a pocketful of nembutals, you did not have to tell them where you got them. I think the only offence in this regard then was to sell them if you were not selling them by prescription, and you could be charged then under the Food and Drugs Act in respect of that illegal sale.

This was not very satisfactory because there was not a very strong penalty applied in these cases. The matter grew to considerable proportions in certain cities in Canada. In view of this circumstance the Food and Drugs Act was amended to provide for schedule G.

Now before you can sell a barbiturate you have to have a licence, from either the province to practice medicine or to practice pharmacy, and as a manufacturer, importer or wholesaler you must be licensed by the Department of National Health and Welfare, in order to deal in these drugs. In addition, you must keep thorough records of what you buy and what you sell and to whom you sell, so that this makes it possible for the department with a proper staff to examine the records at the wholesale, retail and manufacturing level and to audit them and give the information to the department which can be examined to see that the manufacturers are accounting for the products they buy and the ultimate sales to the various people. I think there is no doubt about this having had a satisfactory effect in lessening, if not altogether stopping this illicit traffic in such things as barbiturates and amphetamines. Mr. Hammond will know the details of this.

The CHAIRMAN: Would you like to hear from Mr. Hammond in this regard, Doctor Harley?

Mr. HARLEY: I will leave that to the committee.

The CHAIRMAN: We will hear from Mr. Nicholson first.

Mr. NICHOLSON: In the report of the special committee of the Royal College there appears the recommendation that more testing be done by universities and by research councils in order to assist you in your work. Are you using universities in this regard now, Doctor Morrell?

Dr. MORRELL: Are you referring to clinical testing?

Mr. NICHOLSON: Yes.

Dr. MORRELL: I think the manufacturers have succeeded in getting some of the universities to take an interest in the clinical testing of new drugs.

Mr. NICHOLSON: Does your department use the facilities of universities in this regard at all for clinical testing?

Dr. MORRELL: No.

Mr. NICHOLSON: Do you use these facilities if there is a dispute of any kind?

Dr. MORRELL: We do not do clinical testing, Mr. Nicholson. This is a responsibility of the manufacturers. If we do not like the manufacturer's clinical test we tell the manufacturer or hold up his drug application which forces the manufacturer to do further work in this regard.

Mr. NICHOLSON: Have you any idea of the extent to which manufacturers and pharmacists are using the facilities of universities for clinical testing?

Dr. MORRELL: I cannot give you any figure as to the extent.

Mr. NICHOLSON: Is there any member of your staff who would have that information?

Dr. L. I. PUGSLEY (*Associate Director*): We have not any records of the extent to which this is done, but normally hospitals and hospitals attached to universities do the clinical trials in the majority of instances.

The CHAIRMAN: I would think that when the pharmaceutical association appears before us we will receive more detail in this regard.

Mr. ORLIKOW: Mr. Chairman, before we hear from Doctor Morrell's assistant, I should like to point out that I have a report before me from a committee of the Canadian medical association on pharmacy which was made I think last year or the year before, in which they suggested that the special controls on barbiturates and amphetamines, which were put in for what would appear to be good reasons, have in fact induced doctors to write prescriptions for alternatives for which in fact we know there has been less clinical testing and in respect of which we know less, and we may be worse off in some ways than we were before. I am not an expert and am just attempting to summarize what is said in this report. I know that these matters are not too easy to deal with but I am wondering in the light of our experience since these regulations were amended, whether any thought has been given as to the results.

Mr. R. C. HAMMOND (*Chief of the Narcotic Control Division*): Mr. Chairman, undoubtedly there may be some occasions where physicians may decide to use another type of drug other than a controlled drug, but there is nothing in the legislation or our controlling measures which in any way deters the physician from using these drugs for medical purposes. We have had no indication that to any extent the physicians have been concerned in this way. In fact, the evidence has been just the opposite. We have heard many remarks emanating from the profession which indicates that they welcome the control.

Mr. ORLIKOW: I was not trying to suggest the opposite, but only wanted to suggest that some of the drugs which are being used instead of barbiturates or amphetamines are not subject to the same controls. In other words, a patient does not have to get a new prescription every time. Does this situation create a problem?

Mr. HAMMOND: It is possible that some problems have been created in this regard.

Mr. HAIDASZ: Mr. Chairman, I should like to ask the director a question in respect of imported drugs. Are there any provisions in the act or regulations which require the food and drugs department to carry out the provisions of investigating a drug such as apply to drug manufacturers in Canada?

Dr. MORRELL: Are you speaking of new drugs or any drug?

Mr. HAIDASZ: I am referring to new drugs and any drugs that are imported. Are they subject to the investigations in respect of drugs manufactured in Canada?

Dr. MORRELL: There are several classes of drugs that are dealt with in different ways. If it is a new drug that has been developed in a foreign country,

and that might include the United States, very often a great deal of the investigative work is done in the foreign country. This is the country in which the manufacturer has his research staff and has his hospital and university connections, and it becomes a matter of habit and custom for him to carry out the basic work at least in that country. In many cases when a new drug submission comes in we find that little if any clinical or pharmaceutical testing has been done in Canada. We have been asking for ten years or more that such a drug be tested in Canada, certainly clinically. That is, we have asked that some testing be done here. I think that as a result of the pressure that we have exerted over the years, more and more clinical trials are being carried out in Canada.

There is nothing in the act or regulations that demands that clinical trials must be carried out in Canada.

In respect of ordinary drugs or drugs that are not classed as new drugs, and there are those that are manufactured, as I said before, under licence, and I refer now to those that are listed in schedules C and D of the act, including such drugs as have been listed in schedule C, liver extract injectable, liver extract injectable with other medication, liver extract injectable crude, liver extract injectable crude with other medication, insulin, insulin made from zinc-insulin crystals, globin insulin with zinc, insulin zinc suspension, N.P.H. insulin, isophane insulin, protamine zinc insulin, anterior pituitary extracts and radioactive isotopes and under schedule D, living vaccines for oral or parenteral use, drugs prepared from micro-organisms or viruses for parenteral use, sera and drugs analogous thereto for parenteral use, and antibiotics for parenteral use; these can only be sold in Canada by a manufacturer licenced by the department under the Food and Drugs Act to do so. This implies that before they receive a licence their premises, personnel and facilities are inspected by departmental inspectors making visits.

Mr. HAIDASZ: Do the inspectors visit Europe?

Dr. MORRELL: The inspector makes a visit to Europe if the manufacturer is in Europe and to the United States if it is manufactured in the United States. The inspector then makes a report which, if satisfactory, leads to the renewal of a licence. If it is a new drug that is to be licenced it must be a new drug submission. That means they must be inspected before they can get their licence. After this process is completed, then they may be licenced if the report of the facilities and all the rest of it is satisfactory and up to our standards. So that in that case I would say that the control of the foreign manufacturer is nearly equivalent to that of the domestic manufacturer. I say "nearly" because perhaps he is not quite as close and does not get as frequent inspections. The foreign manufacturer is usually inspected once a year, and certainly not less than once every two years. The local manufacturer in Canada or in the United States who has a licence is certainly inspected every year. The foreign manufacturer is inspected not less than once every two years, certainly every two years or more frequently.

In respect of the other drugs, the general pharmaceutical specialties, we do not have the authority to require, in our regulations, an inspection of the premises, and our studies must be made on the product as it reaches Canada.

Have I made myself clear?

Mr. HAIDASZ: Yes. I should like to ask a supplementary question. In your view, Doctor Morrell, do you not think that in the interest of Canadians and in fairness to the Canadian pharmaceutical manufacturers, all imported drugs should undergo the same review as domestic drugs?

Dr. MORRELL: Yes, essentially I think that is correct, and the Food and Drugs Act really applies equally to any product sold in Canada whatever its origin. I think that is essentially correct.

Mr. HAIDASZ: These regulations are not in force yet?

Dr. MORRELL: We do not have them as yet, no.

Mr. HAIDASZ: Do you think such regulations should be in force?

Dr. MORRELL: Yes, I think it would be very useful to have such regulations in force.

Mr. VALADE: Is it possible, Doctor Morrell, to have the same treatment, tests and conditions which apply in this country apply to foreign manufacturers of drugs?

Dr. MORRELL: Are you referring to the same inspection procedures, for example?

Mr. VALADE: Yes.

Dr. MORRELL: I think it should be possible if they want to sell their drugs in Canada. I think they should be prepared to undergo the same controls as apply in respect of our domestic manufacturers.

Mr. VALADE: My question is based on the potential possibility that in a country of say 40 million people there certainly would exist a greater possibility for clinical tests than in this country of only 18 million people with perhaps a proportionate number of medical people.

Dr. MORRELL: I suggest this depends on the country you refer to, sir. I have been in countries where there are four or five times the number of people that are in Canada and I can assure you that the controls are nowhere near as rigid as ours. However, in other countries which are smaller their tests and controls are as good as ours.

Mr. VALADE: I should like to ask a follow-up question in respect of a subject referred to earlier. I think you said before that your department licensed drugs and not manufacturers?

Dr. MORRELL: I think that is correct.

Mr. VALADE: I am wondering whether it would be advantageous in respect of the control of drugs to have your department license drug manufacturers as well as drugs. This would not remove the control or licensing of drugs themselves but would add to the control by the imposition of certain responsibilities upon manufacturers under licence, making them subject to the normal rules and regulations.

Dr. MORRELL: Are you suggesting that the manufacturer should be licensed for all of his products?

Mr. VALADE: Yes, and then that would not, as I say, cancel out the requirements for licensing drugs individually.

Dr. MORRELL: The basic legal question here could be answered by Mr. Curran.

Mr. CURRAN: On this question of licensing the manufacturer Mr. Baldwin might have something to say. Our legislation is the criminal law and it does not include the right for licensing a trade or a profession. We can license a product under particular conditions, as we have done, but the general licensing of the trade under the criminal law statute is not within our constitution.

Mr. VALADE: I thought that we licensed the medical men and by licensing them we also licensed some medical corporations or medical organizations such as the Royal College of Physicians and Surgeons in the provinces of Ontario and Quebec.

Mr. MONTEITH: That is a provincial matter.

Mr. VALADE: Yes, but would this involve only provincial legislation or could it be done under federal legislation?

Mr. CURRAN: In my view it would have to be done under provincial legislation, unless we changed the whole basic structure, in which case we would get into a trade and commerce type of clause which means the provincial movement of products. At the present time we are working under the criminal law which has universal application in Canada, and if we change the basis we change the whole structure of the control.

Mr. VALADE: I have another question. Dr. Morrell said before that his department has no legal authority to act in regard to offences against the rules set by his department. Is that correct? Have you no authority to implement or to stop the distributor of drugs or to stop a drug from being put on the market if you feel that there might be danger in it? Is it true that you can just advise but that you do not have the power to enforce this?

Dr. MORRELL: In the amendment that was passed last fall we have certainly asked the minister to put that drug on schedule H which prohibits its sale entirely.

Mr. VALADE: But only if it is on that schedule?

Dr. MORRELL: There are other applications of this. If a product violates some section of the existing regulations of the act—let us forget schedule H—then we have the power to seize it. For example, if a drug was found not to meet the standard under which it is sold, and it might be twice as strong in which case it is dangerous, we do have the power to seize these tablets or whatever they are and to have them destroyed or reworked. However, it must violate some section of the act or some regulation. It is not because I do not like it or I am afraid of it, but it must meet the requirements of the law, and what we are here to do is to enforce the law as it exists. This is what we have tried to do.

Mr. VALADE: I asked that question because I think it was not clear.

Mr. MONTEITH: I think it is fair to say, Mr. Chairman, that Dr. Morrell does put before me every once in a while a submission that a certain quantity of a certain drug, picked up under certain circumstances, which is other than as advertised, should be destroyed, and this is done.

The CHAIRMAN: Before you go ahead, Dr. Horner, I should ask whether it is in accordance with the wish of the committee that we close this meeting at 12:15.

Mr. NICHOLSON: Do we reconvene this afternoon?

The CHAIRMAN: Let us discuss this at 12:15.

Mr. HORNER (*Jasper-Edson*): I would like to clarify the legal position here. As I understood it earlier, all patent medicine manufacturers are registered or licensed.

Dr. MORRELL: That is a voluntary thing. You do not have to register a product but you may go and ask for registration.

Mr. HORNER (*Jasper-Edson*): Let me get this clear. I can go out, make a concoction and peddle it to drugstores without registering it with your department and without having a licence from you?

Dr. MORRELL: That is correct.

Mr. HORNER (*Jasper-Edson*): How can your department have any control over patent medicines or other medicines?

Dr. MORRELL: You can make this concoction you are talking about and sell it to a drugstore. As soon as we know there is such a concoction on the market we would certainly take an interest in its composition and so forth. If we are not satisfied, then we can exert certain restrictions on the sale of that product. But if you want to make that concoction and go to the department and

ask for its registration, consideration will be given to whether or not it is proper to register it under the Proprietary Patent Medicine Act.

Mr. HORNER (*Jasper-Edson*): May I ask you a further question in this regard? Do you not feel that your department and your directorate would have a better opportunity to police the drugs if all manufacturers of drugs were licensed even as to product? In other words, anyone who makes anything for medicinal purposes has to be licensed with your department. Is this unconstitutional?

Mr. CURRAN: Mr. Chairman, this is a very complicated field and I do not like to give an opinion on this. There are many ways in which controls can be exercised short of absolute licensing. Normally the licensing of a manufacturer would be a matter for provincial consideration, and I distinguish here between the agricultural statutes which proceed under a different basis. In the case that Mr. Horner has mentioned, it would have to comply with the Food and Drugs Act and all the conditions of the act including suitable conditions of manufacture and all controls which are applicable to all drugs. Therefore, it is not quite as easy as suggested for anyone to come along and put a concoction on the market. He is still subject to the Food and Drugs Act, and he is subject to all of the controls of the Food and Drugs Act including prosecution and seizure if his product violates any of the provisions of the act. Licensing by itself would not necessarily do any more than is being done at the present time under the elaborate control which the act provides. In case of proprietary patent medicines, it is a voluntary matter with the manufacturer. If he wishes to sell his product under a registration number, this is his choice. The product is then scrutinized, and if Mr. Soucy and the food and drug authority are agreeable that the product has therapeutic values, then registration can be given. However, it is a voluntary matter with the manufacturer. Otherwise he can market his product only subject to the rigid controls of the Food and Drugs Act.

Mr. BALDWIN: I have a supplementary question on that issue. I also think that such a person would be subject to the provision under the Criminal Code which deals with deceptive and improper advertising, so that if claims were made which were not correct then this person could be prosecuted under criminal law.

Mr. CURRAN: That is correct. I think it is section 3 or 7, which provides it to be an offence if a person should advertise a product for the purpose of stimulating its sale and makes claims for it that have not been subject to adequate and proper tests. The onus is on the accused to show the adequate and proper test to which a product has been subjected. It is also subject to the provisions of the Food and Drugs Act. There are therefore two statutes which would govern this situation.

Mr. VALADE: The department has some inspectors whose duties are to check into all the distributing sources and to report to your directorate on new drugs, patent medicines and things of that nature. Is that not so?

Mr. CURRAN: That is so.

Mr. HARLEY: I have two questions; the first one I will put to Dr. Morrell. Could he tell us the method by which heroin was taken off the market? This is apropos to what Mr. Valade was asking.

Dr. MORRELL: I will ask Mr. Hammond.

Mr. HAMMOND: Mr. Chairman, the story behind this is that the world health organization recommended that the use of heroin be restricted. I think it was in 1954 or 1955, I am not sure, but from that date on we did not issue any further permits or licences permitting the importation of supplies into Canada. The fact is that we still have supplies in Canada and they are not being used. With the changing events in medicine there has been a change from heroin to other analgesics.

Mr. HARLEY: If a hospital wishes to acquire some of this drug is it still available?

Mr. HAMMOND: Supplies are still available. It might be difficult to get it in an exact strength of tablet, but there are supplies available.

Mr. NICHOLSON: Before I reach the question I originally intended to ask, I should like to direct a question to Mr. Curran. I refer to a concoction of the kind Dr. Horner speaks about; in order for it to come within the definition of a patent medicine, it would have to be patented, would it not?

Mr. CURRAN: I do not wish to get into historical events, but originally the definition of a proprietary or patent medicine did contemplate a question of patent.

Mr. NICHOLSON: Yes.

Mr. CURRAN: Under the enactments of today, most of these products are not patentable and the commissioner of patents does not issue a patent in respect of these products. In the first place, you do not patent a product, you patent a process, and in this sense a patent medicine would not come within the criteria which is associated with the issuance of a patent. In other words, there is no machinery or method for making a preparation which would be patentable. As I say, this is an obsolete expression which we have not as yet stopped using.

Mr. NICHOLSON: Thank you. The other question I wish to ask is a follow-up to a question asked Dr. Morrell earlier as to whether or not there is some advantage in having a clinical evaluation carried on by an impartial body such as a university or competent medical school. Am I right that such a recommendation was mentioned by the special committee of the Royal College?

Dr. MORRELL: Yes, I think you are right, Mr. Nicholson.

Mr. NICHOLSON: Would you agree that there is some advantage in adopting such a procedure?

Dr. MORRELL: Yes, I think there would be some advantage in that regard.

Mr. NICHOLSON: Thank you.

Mr. ORLIKOW: Mr. Chairman, there has been reference to the serious problems in respect of the use of prescription drugs because of the proliferation of these drugs. These drugs would not be produced and sold if they were not being used, and they could not be used if the doctors did not prescribe them. Doctors will only prescribe them after they have received information about them. This results in a fantastic amount of advertising being sent to doctors. I wonder whether the department has given any consideration to modifying or regulating the type and amount of advertising which drug companies can use. I am told that the *Canadian Medical Association Journal* has been used in regard to this problem, but I understand that no real solution has been found.

Mr. MONTEITH: Mr. Orlikow, if I may just interject before Dr. Morrell answers your question, I should like to point out that there was an amendment to the act last autumn which actually prohibits the distribution of samples as advertisement without the practitioner writing or signing some sort of request for such samples. In regard to the actual advertising material, I think perhaps Dr. Morrell can give you an answer.

Dr. MORRELL: There is a prohibition in the act which prohibits any person from advertising a drug in a manner that is false, misleading or deceptive, or likely to create an erroneous impression regarding its value, merit or safety. We have certainly done our best to apply this section of the act in respect of advertising of drugs to the general public. We do this daily and I know that between 30,000 and 35,000 radio and T.V. commercials were examined last year in respect of foods as well as drugs.

We have the prohibitory section in the act itself, being section 3, which I think is unique in the Canadian Food and Drugs Act. It states that no person shall advertise any food, drug, cosmetic or device to the general public as a treatment, preventative or cure for any of the diseases, disorders or abnormal physical states mentioned in Schedule A, and no person shall sell any food, drug, cosmetic or device that is represented by label, or that he advertises to the general public in that way.

Schedule A contains a lot of rather serious diseases or disorders. That prohibits, whether the advertising is honest or dishonest, the advertising of them because the diseases and disorders that are mentioned are of such a nature that proper diagnosis is necessary for the public to know whether they have such a disease, and proper supervision and treatment as well as prescribing are necessary if one is to get any advantage from the drug that is taken. If the advertisement can persuade people to treat a pain in their chest or stomach with such and such a product it may be that they are treating something that they have not got, and what they have got is serious enough that when they get around to going to the doctor it is too late. I think that in itself is a very favourable section of the Food and Drugs Act, and this is certainly enforced.

When you come to a discussion regarding advertising to the professions, we have in the past been rather loath to interfere with that advertising to the medical profession. We have been rather loath to interfere in this field because we feel that these people have been trained and are experts and will themselves recognize falsehoods or puffery. In other words, they can take care of this. However, we have not entirely refrained from taking steps in the case of antibiotics which had serious reactions in children and some adults, and we require the manufacturer in his promotional material to include a carefully worded statement about these reactions.

It may be that we need to go further in regard to advertising directed to the general public, and I might say that the Canadian medical association itself has set up a code. I do not know whether at the moment it is actually in use, but we have seen this code and have commented on it for the Canadian medical association. It seems to be a reasonable code. The intent of it, of course, is that it must meet the code as set forth before it will accept advertisements for its journals.

Mr. ORLIKOW: My information is that this code is not yet in effect, but it seems to me that doctors are deluged by so much material, competent as they may be, they just do not have time to really sort it out, and it may be that the department should do some of this sorting for them. I do recognize that there are difficulties involved.

The CHAIRMAN: I may point out that Doctor John O. Godden, associate editor of the *Canadian Medical Association Journal* is one of the witnesses we propose calling. He may be able to give some information in this regard.

Mr. RYNARD: Mr. Chairman, a part of my question has been answered, but I should like to ask Doctor Morrell if it is not true that in light of the advertising that goes out by these firms to doctors, there is a great deal of useful information in respect of tests carried on in universities and other well equipped clinics of great use to doctors in evaluating the drug being advertised?

Secondly, I should like to state that any doctor can acquaint himself with a therapeutic index which lists all those drugs, in order to make a comparison of the advertisements that are received. I do not know whether there is such a therapeutic index in existence in Canada, but there certainly is one available in New York through which one can check these drugs, their uses, abuses and so forth. I just wanted to bring that point out and suggest that a great deal of useful information is contained in many of the advertisements received as a result of clinical trials of these drugs under proper supervision.

Mr. PATTERSON: Mr. Chairman, I should like to ask one question based on a reference in the minister's statement which he delivered at the beginning of this meeting regarding the discussions that are carried on between himself and the provinces in regard to the rehabilitation of thalidomide babies. I wonder whether he could just inform us as to the status of these discussions at the present time?

Mr. MONTEITH: Actually at the time we requested such discussions we found that the records in respect of deformed children, if you wish to call them that, in the provinces are very incomplete. There was really no record kept in any province concerning this matter. It was suggested that we undertake a system of reporting these cases. I realize there are difficulties involved, and I am assuming that perhaps the doctors will be able to speak to this subject. I realize, of course, that they are loath to give private medical information on occasions, but it was hoped that we could acquire better statistics concerning cases of malformed children.

Now, as far as thalidomide itself is concerned, we have had reports from British Columbia, Manitoba, Ontario, Nova Scotia, Prince Edward Island and Newfoundland. There are 31 cases reported from the provinces that I mentioned, six of them are mild, 12 are moderate and 13 severe. We have some later figures which have come in: Alberta 4, all severe, Saskatchewan 6, three severe and three mild. There has been a report from Quebec of 70 unclassified cases. There were no cases in New Brunswick and Prince Edward Island. At the time of the Federal-Provincial Conference in August, the government offered to participate in 50 per cent of any projects brought forward by the provinces for the assistance of these cases. I do not think we have any project before us as yet but I understand there are some coming forward.

Mr. PATTERSON: I have one supplementary question: does this include all malformed babies or just the thalidomide babies?

Mr. MONTEITH: Is it safe to say, Dr. Cameron, that we suspect the 70 cases from Quebec include some generally malformed babies as well as babies where thalidomide may have been involved? We do not have any real figure.

Dr. CAMERON: The Quebec investigation is still going on. These are not classified cases. These are deformed children in various degrees of deformity, and the question is whether or not they are associated with thalidomide. I understand this has not been settled. The others listed by the minister are associated with thalidomide to the best of our knowledge.

Mr. PATTERSON: Does the assistance program you have outlined, Mr. Monteith, include all deformed children?

Mr. MONTEITH: No, it includes only those definitely tied in with thalidomide. Dr. Cameron, would you like to supplement that answer?

Dr. CAMERON: I was just going to remind you that at the meeting with the provinces on August 17 two proposals were made for the department to follow up. One proposal was the establishment of a committee to look into the best methods of dealing with deformed children, with particular reference to thalidomide. That committee was established, it did its job, it made its report, and the program is now under way to acquaint orthopedic surgeons and others in this country with the most up to date methods of dealing with these children. It is recommended that three centres be established for dealing with these children.

Mr. MONTEITH: This was tabled last Friday.

The CHAIRMAN: I will get you all a copy of the report, if you wish.

Dr. CAMERON: I do not need to go into the details, as the chairman says, because it is in that report. Funds have been authorized to carry out that program.

The other recommendation was that a study be made of our methods of obtaining precise information about birth deformities in this country. This is not satisfactorily obtained at the present time because the deformities are of many different kinds, and on occasion it is not possible at birth or when birth registration is made to determine whether a child is possibly deformed internally and the degree of the deformity. If we are going to get good information, we have to have a more elaborate system. That committee has met and that study is going forward. We see it is absolutely essential, if we are going to advance our knowledge of the possible deleterious effect of drugs and other substances that surround us, that we have better knowledge of what has actually taken place. Those two committees have met and the job is under way.

The CHAIRMAN: Gentlemen, it is past 12:15. There are three things I would like to take up before we adjourn. I would like to have a motion that the chart of the food and drugs directorate be printed as an appendix to this day's minutes of proceedings and evidence. May I have that motion?

Mr. FAIRWEATHER: I so move.

Mr. HAIDASZ: There should be an explanation in regulation C.01.013 on page 77 because it is not followed by numbers up to C.01.021. In other words, there seem to be eight regulations missing on page 77.

The CHAIRMAN: I am only talking about this chart. I do not intend to have the Food and Drugs Act and regulations printed.

Mr. HORNER: I second the motion.

Motion agreed to.

The CHAIRMAN: The next problem is that we do not have enough copies of the proceedings. An additional motion is required. The motion should read that the number of printed copies of the meetings of the committee of the proceedings and evidence in English, including issue No. 1, be increased from 750 to 1,500 and that a sufficient number of copies be made available to the chairman of the committee for mailing purposes. These would be mailed merely to witnesses who may be called and not for my own use I may say.

Mr. NICHOLSON: I so move.

Mr. HARLEY: I second the motion.

Motion agreed to.

Mr. ORLIKOW: I hope you are going to make sure that not only people who are witnesses but people in university departments and so on who are directly concerned will be getting this. I do not suppose we can cover everyone.

The CHAIRMAN: I might point out one thing. I am going to try to send this list to the people we propose to call. I really do not think we can mail it to every university and every doctor in the country. I think it would not be proper. They can get in touch with the Queen's Printer and get it at their own volition.

Mr. ORLIKOW: Will that be mailed from day to day?

The CHAIRMAN: We are trying to arrange it.

The other motion is that permission be sought from the house for the committee to meet in Montreal, Quebec on Thursday, Friday and possibly Saturday, February 14, 15 and possibly 16, 1963, and that the clerk of the committee accompany the committee to Montreal. This is only to get permission from the house so that we can make our trip.

Mr. ORLIKOW: I was not here at the last meeting. Is the trip for the purpose of inspection?

The CHAIRMAN: Yes, the Hotel Dieu hospital, clinical research division, Ayerst, McKenna and Harrison Limited, and Charles E. Frosst and Company in Montreal.

Mr. NICHOLSON: You were going to give consideration and advice today on whether or not we should visit the Ciba premises.

The CHAIRMAN: I might say, with regard to this motion, that the people I called long distance felt that two and a half days would be squeezing it to see that, and if an additional meeting or trip was contemplated it should be done at the time. Can we have a motion?

Mr. PATTERSON: Was that not covered at the last meeting?

The CHAIRMAN: I have to have an official motion so that I can go before the house and ask permission to do this.

Mr. ORLIKOW: I so move.

Mr. HORNER (*Jasper-Edson*): I second the motion.

Motion agreed to.

Mr. NICHOLSON: Speaking of the list of witnesses to be called, I may say that the head of the neurological research division of the university of British Columbia has suggested that this committee give consideration to calling Dr. George Ling, assistant professor of the department of pharmacology. He is not only a brilliant scientist but he has spent years in the drug industry, both in research and in sales. I think he would be a worthwhile witness.

The CHAIRMAN: I will get this down.

The other point was about the future sittings. My own view was that we should not sit this afternoon. We should sit on Thursday at 9.30 a.m. to continue our discussion with the minister and the directorate officials. Is that in accordance with the wishes of the committee?

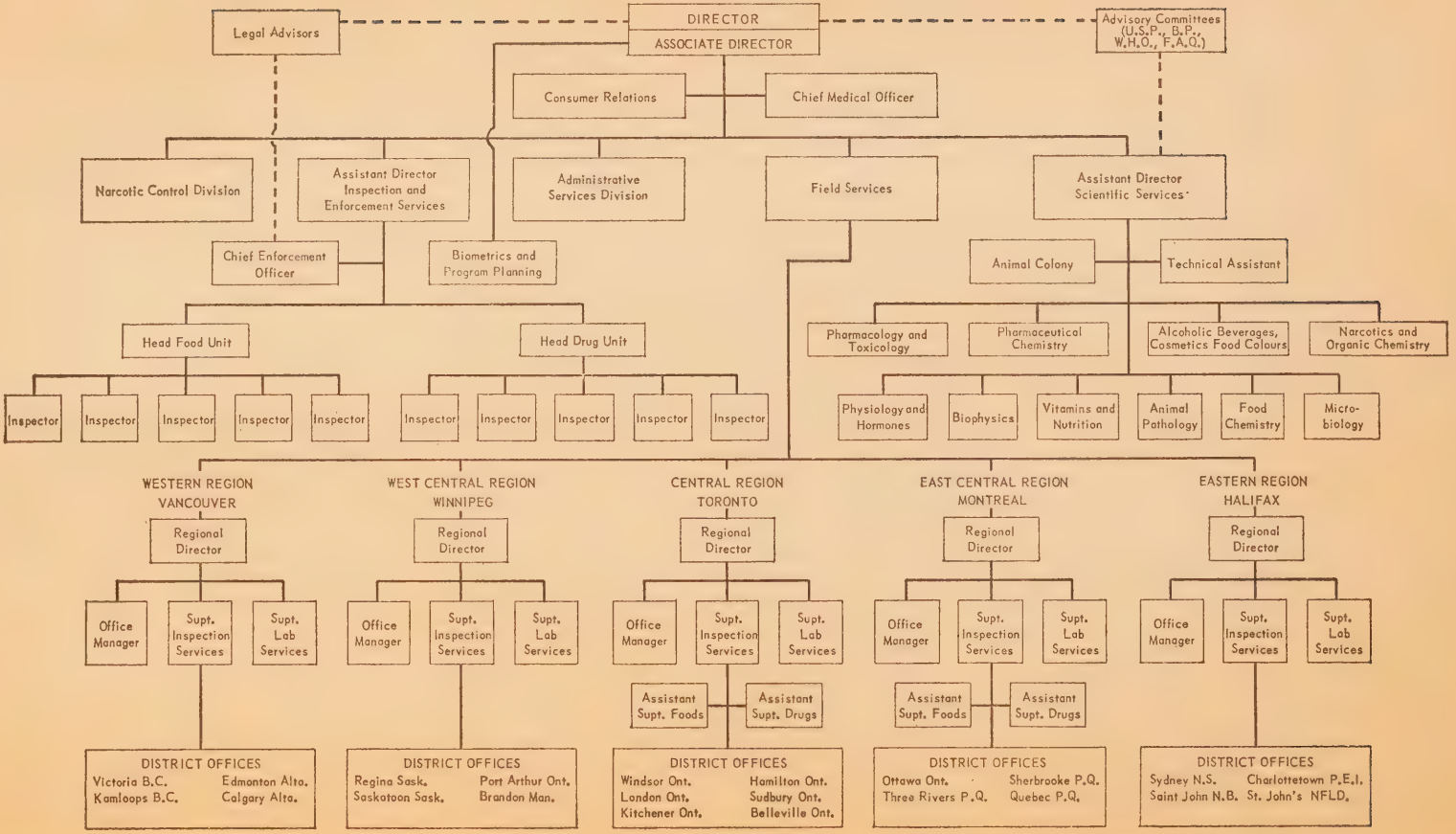
Mr. HARLEY: Did you call other witnesses for Thursday?

The CHAIRMAN: No. Is that agreed? The other thing is that the special committee on drugs of the Royal College of Physicians and Surgeons headed by Dr. Brien, will be available at 9.30 next Tuesday morning and I think he will have the other two members of this committee with him. These people are very busy men and I propose that that day we sit from 9.30 a.m. to 12.30 and after Orders of the Day until 5.30 so that we might try to get this report cleaned up in that one day so that these men can go back to their universities.

Any other business? The meeting is adjourned until 9.30 Thursday morning.

APPENDIX "A"

THE FOOD AND DRUG DIRECTORATE



OFFICIAL REPORT OF PROCEEDINGS AND EVIDENCE

This edition of the Minutes of Proceedings and Evidence contains the text of Evidence in the language in which it was given, and a translation in English of the French texts printed in the Evidence.

HOUSE OF COMMONS

First Session—Twenty-fifth Parliament

1962-1963

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. R. M. T. McDONALD

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 3

THURSDAY, JANUARY 31, 1963

WITNESSES:

Dr. C. A. Morrell, Director; Dr. J. B. Murphy, Chief Medical Officer; Mr. R. C. Hammond, Chief of the Narcotic Control Division, all of the Food and Drug Directorate, Department of National Health and Welfare; Dr. G. D. W. Cameron, Deputy Minister of National Health; and Mr. R. E. Curran, Legal Adviser, Department of National Health and Welfare.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1963

28313-5—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. R. M. T. McDonald

Vice-Chairman: Mr. Georges Valade

and Messrs.

Baldwin	Harley	Martin (*Essex East*)
Enns	Horner (*Jasper-Edson*)	Mitchell
Fairweather	Howard	Nicholson
Haidasz	Marcoux	Patterson
		Rynard—15

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

NOTE:—Mr. Orlikow was replaced by Mr. Howard prior to the fourth meeting.

ORDER OF REFERENCE

HOUSE OF COMMONS
TUESDAY, January 29, 1963.

Ordered,—That the name of Mr. Howard be substituted for that of Mr. Orlikow on the Special Committee on Food and Drugs.

Attest.

LÉON-J. RAYMOND,
Clerk of the House.

28313-5—1½

MINUTES OF PROCEEDINGS

THURSDAY, January 31, 1963.
(4)

The Special Committee on Food and Drugs met at 9.50 a.m. this day. The Chairman, Mr. R. M. T. McDonald, presided.

Members present: Messrs. Baldwin, Haidasz, Harley, Howard, Horner (*Jasper-Edson*), McDonald (*Hamilton South*), Mitchell, Nicholson, and Rynard. (9).

In attendance: From the Department of National Health and Welfare: Dr. G. D. W. Cameron, Deputy Minister of National Health; Mr. R. E. Curran, Legal Adviser; Mr. Eric Preston, Chief Personnel Services; Mr. D. H. Dunsmuir, Executive Assistant to the Minister: *from the Food and Drug Directorate:* Dr. C. A. Morrell, Director; Dr. L. I. Pugsley, Associate Director; Dr. R. A. Chapman, Assistant Director in Charge of Scientific Services; Dr. J. B. Murphy, Chief Medical Officer; Mr. M. G. Allmark, Chief of the Pharmacology and Toxicology Section; Mr. Paul Soucy, Chief of the Proprietary or Patent Medicines Section; and Mr. R. C. Hammond, Chief of the Narcotic Control Division.

A quorum being present, the Chairman welcomed Mr. Howard, a new member of the Committee.

With permission of the Committee, Dr. Morrell read a short statement being a summary of the action taken by the Department about the drug Liefcort; this information was asked for at a previous meeting. He was questioned thereon and was assisted by Dr. Murphy.

Dr. Morrell was also questioned about the application of the Rules of the Food and Drugs Act to the vitamin preparations, and about commercial advertising of drugs.

At 10.45 a.m., the Committee agreed to take a short recess.

At 11 o'clock the Committee reconvened.

Mr. Hammond, Dr. Cameron and Dr. Morrell answered questions about controlled drugs and narcotics.

Following a request made by members at a previous meeting, Mr. Curran explained the federal-provincial responsibility with regard to licensing. He and Dr. Morrell answered questions thereon.

Before adjournment, the Chairman announced that the members of the Special Committee of the Royal College of Physicians and Surgeons will appear before the Committee on Tuesday next, February 5, at 9.30 a.m., and that a meeting has been arranged for the Canadian Pharmaceutical Manufacturers Association to appear on March 5th.

It was agreed to ask the Associations who wish to be heard to supply the Committee with copies of their briefs beforehand, so that the Members have a more comprehensive hearing.

At 11.30 a.m. the Committee adjourned to Tuesday, February 5, at 9.30 a.m.

Gabrielle Savard,
Clerk of the Committee.

EVIDENCE

THURSDAY, January 31, 1963

The CHAIRMAN: I see a quorum. Gentlemen, I would like to welcome Mr. Frank Howard to our committee. He is replacing Mr. Orlikow today.

At the last meeting there were some questions asked and I believe Dr. Morrell would like to make a statement in respect of these questions. The first question, I believe that I posed, was followed up by Dr. Horner and Dr. Haidasz. This was with regard to Liefcort and Dr. Liefmann. I wonder if Dr. Morrell could bring us up to date on the procedures the department took in respect of this drug. He might give us a brief resume.

Dr. C. A. MORRELL (*Chief of Food and Drug Directorate*): Mr. Chairman, the attention of the food and drug inspectors was drawn to Liefcort through a popular article in a newspaper, in which it was indicated that a new treatment for arthritis had been discovered. The food and drug inspectors immediately visited Dr. Robert Liefmann and explained to him the requirements of the Food and Drugs Act in respect of the introduction of a new drug for clinical trials. Dr. Liefmann was advised in writing that he must comply with the requirements of section C.01.307 of the food and drug regulations. Dr. Liefmann agreed to do so.

Since some time is necessary to obtain the results of clinical trials in such a case, Dr. Liefmann was allowed several weeks in which to obtain these reports from his qualified investigators. After this period of time had elapsed, our inspectors returned to Dr. Liefmann to assure themselves that he was, in fact, carrying out all the requirements of section C.01.307. On the occasion of this second visit, it was observed that not all of the requirements had been adhered to and once more, Dr. Liefmann was advised of what he would be expected to do. He again promised to adhere to the provisions of the regulations.

At this time it was also learned that Dr. Liefmann had not given us the facts about the true nature of the product and it was necessary for us to analyze it in our own laboratories. Although Dr. Liefmann felt that the reports from the investigators he selected were adequate, we could not agree with him that they would be suitable for inclusion in a new drug submission which, of course, is the purpose of clinical trials on new drugs that are still in the investigational phase. Our inspection of his records of distribution and of the reports received, showed them to be quite incomplete in complying with the requirements of section C.01.307.

Several subsequent visits at short intervals by our inspectors indicated no improvement from our point of view and finally, a letter was written to Dr. Liefmann demanding that no further distribution of the drug to investigators be made.

Dr. Liefmann agreed to cease further distribution and informed us that Endocrine Research Laboratories had ceased to exist. Subsequent investigations have indicated that Dr. Liefmann is confining his activities to his own private practice and no products labelled as Liefcort are being given to his patients.

That is the summary of action taken by the department in respect of the drug.

The CHAIRMAN: Are there any questions on that?

Mr. HARLEY: I was going to ask Dr. Morrell whether the United States food and drug directorate was involved in this. I understand these products are being given to people from the United States and taken over the border.

Dr. MORRELL: The United States Food and Drug Administration is certainly interested because of the fact that the Americans are importing it for use; but I must point out that he had given no indication to the United States Food and Drug Administration that he was putting out a drug for clinical trial in the United States. In fact, he was not officially doing so, and from that fact alone the importation of Liefcort into the United States would have been in violation of the Food, Drug and Cosmetic Act of the United States. So, of course, they were interested from the administrative standpoint.

Mr. HARLEY: I understand that the drug was actually taken in by a patient who would return to the United States. Does this mean in law that he is not really exporting it by giving it to someone in Canada who takes it over himself?

Dr. MORRELL: I believe this did happen; that they came to his office in Montreal and took a lot of the drug back. I believe this happened frequently.

Mr. HAIDASZ: Did I understand your last two sentences correctly; that he may give this drug to his patients?

Dr. MORRELL: In so far as the Food and Drugs Act is concerned, I think he may. I do not know of any authority in the Food and Drugs Act to tell him he may not.

Mr. HAIDASZ: Did the department analyse the constituents of the drug Liefcort, and what were the results of the analysis?

Dr. MORRELL: I said it was analysed.

Mr. HAIDASZ: By whom?

Dr. MORRELL: By our laboratory. I think Dr. Stephenson in the food and drug laboratory found it to contain estradiol, methyltestosterone and prednisone.

Mr. HAIDASZ: From the reports we have read in the newspapers, I believe that the laboratory in New York tested the doses of these three drugs in Liefcort and found them to be above the therapeutic dose.

Dr. MORRELL: I think I have seen this report to which you refer, and that dose of estradiol was ten times the usual dose. It is difficult to say it is never given by a doctor in the dose that is in Liefcort, but the dose of estradiol at least is higher than the usual dose suggested.

Mr. HAIDASZ: Were these same results obtained by your laboratory?

Dr. MORRELL: Essentially. We got somewhat more than 9 times and they got ten times the usual dose. There was no substantial difference in the results that we heard of eventually from the Food and Drug Administration in the United States and our own.

Mr. HAIDASZ: Is not the Food and Drug Directorate also interested in the several levels of doses of these drugs?

Dr. MORRELL: Yes, in a way, Dr. Haidasz. This was a drug out for investigational trials. As you know, having read C. 01.307, at the moment we do not even have the authority to demand the composition. We found this out by our own analysis. I would say that when a drug is out for investigational use it is a different matter from when the drug is on the market in regular commercial or medical use. It could be that the dose of a drug in investigational use would be higher than usual for a certain condition for which some doctor might think it would be useful.

Mr. HAIDASZ: But the dose of estradiol has already been established for therapeutic purposes; it is not a new drug. The safe levels of the hormone

estradiol have already been established. I do not think he had an excuse in saying that in so far as the dosage of estradiol was concerned he was only experimenting clinically. This has already been established.

Dr. MORRELL: I did not know there was one dose and one dose only used for estradiol.

The CHAIRMAN: Could I have one clarification. Were the researchers or clinical investigators in your view clinical investigators in this instance or was this merely a testimonial?

Dr. MORRELL: The reports we saw were not satisfactory. Many of them were in the nature of testimonials.

Mr. BALDWIN: In respect to Liefcort, as I understand it, it is now on schedule H. Am I correct in that?

Dr. MORRELL: Liefcort is not schedule H. There are two drugs on schedule H, thalidomide and LSD.

Mr. HAIDASZ: Does not Dr. Morrell think that liefcort should be put on schedule H owing to the fact that a dose of estradiol is ten times the therapeutic dose of that hormone.

Dr. MORRELL: Liefcort is not now being distributed to anyone.

Mr. HAIDASZ: Neither is thalidomide nor LSD.

Dr. MORRELL: No, because they are all on schedule H and liefcort is not being distributed because we have told Dr. Liefmann he must not do it.

Mr. HAIDASZ: And yet he is allowed to use it on his patients when you do not allow thalidomide to be used on certain patients.

Dr. MORRELL: Well, we feel that a doctor should be allowed to prescribe in general what he thinks fit because this is the practice of medicine.

Mr. HAIDASZ: There are some doctors who believe they should prescribe thalidomide to some male patients suffering from insomnia.

Dr. MORRELL: Yes.

Mr. HAIDASZ: Why do you allow liefcort to be given at the discretion of a doctor and not thalidomide.

Dr. MORRELL: I think thalidomide is a special case.

Mr. HAIDASZ: Well, I still think you are in a way, as I say, not following your line of judgment in the principle you have set forth, seeing that in the case of thalidomide there are certain useful effects and certain harmful effects and yet you abandon it completely, even at the discretion of clinical researchers.

Dr. MORRELL: Well, it was banned by an act of parliament.

Mr. HAIDASZ: Yes. But, as I say, the minister, upon your advice, can put liefcort on schedule H; it does not have to go to parliament. It is this schedule H that was legislated but not the individual drugs on schedule H.

Dr. MORRELL: We have investigated the distribution of liefcort since the order was given to Dr. Liefmann and we certainly have found no evidence that it is going anywhere else but to perhaps his own patients, and that I do not know for certain.

Mr. HAIDASZ: I think that if you have adopted the solicitude to protect Canadian patients from thalidomide, if liefcort is a dangerous drug you should protect all Canadian patients from liefcort.

The CHAIRMAN: For clarification—as you know, I am not a practitioner—does the food and drug directorate investigate many drugs other than liefcort a year and do they direct the medical profession how to use these drugs?

Dr. MORRELL: I think the introduction of section 14(a) of Bill C-3 was the first time that the Food and Drugs Act was used either directly or indirectly to tell physicians what they may not prescribe.

Mr. HARLEY: Mr. Chairman, I wanted to have a clarification from Dr. Morrell on this one matter. I think he partially has answered the question already. If Dr. Liefmann is able to prescribe the drug, liefcort, to his own patients I assume then he must be continuing to manufacture it himself. In other words, he obtains the ingredients somewhere but combines them himself.

Dr. MORRELL: Yes. As you know, there are three ingredients, estradiol, methyltestosterone and prednisone and he could give his patients the same amount of them separately as he has combined them in this mixture.

Mr. HARLEY: I agree.

Dr. MORRELL: He is mixing them.

Mr. HARLEY: No doubt he buys these things in a more or less raw state from one of the other drug firms and combines them in the proportion he sees fit.

Dr. MORRELL: Yes, and he might even double the dose of estradiol, as far as I know, and I do not think I could prevent him from prescribing any dose of estradiol he saw fit to prescribe.

Mr. RYNARD: Dr. Morrell, did not the status of Dr. Liefmann change? Is he not a licensed physician now; whereas he was not when you first took action?

Dr. MORRELL: He is a licensed physician now, and, as far as I know—and I am sure I am right—at that time he did not have a licence.

Mr. RYNARD: Yes, I do think there is a distinction there. The number two thing is: did he see these patients repeatedly so he could change the dosage, because there is a difference in dosage at the start; you may give a maximum dosage and then bring the patient down to a therapeutic level. I do not think that has been brought out. There is a difference in dosage.

Dr. MORRELL: Yes.

Mr. RYNARD: I wondered whether he had seen these patients.

Dr. MORRELL: We saw a few record cards and some of his patients he saw more than once.

Mr. RYNARD: Did he change the dosage?

Dr. MORRELL: I did not see the cards myself; the inspectors saw the record cards and I do not know whether or not Dr. Liefmann changed the dosage.

Mr. RYNARD: In other words, the drugs that he was combining he might have been buying from a reputable manufacturer and he may have been giving those drugs which every physician uses in his practice. Then I think the question comes up, if he did keep records, did he change the dosage and treat his patients in accordance with therapeutic law. Certainly if he is a registered physician now there has been quite a difference in the picture because previously he was not.

Dr. MORRELL: He was a graduate in medicine, you understand.

Mr. RYNARD: But he was not licensed.

Dr. MORRELL: No.

Mr. RYNARD: Is that correct?

Dr. MORRELL: As far as I know that is correct.

Mr. HORNER (*Jasper-Edson*): I think the main thing is that, in fact, this is not a new drug but rather a combination of old drugs.

Dr. MORRELL: Yes and I am not sure it is a brand new combination; it is certainly a combination of well known drugs.

Mr. HOWARD: Is it true that, as in the case of liefcort, there are combinations of other drugs that go into making up thalidomide and lysergic acid?

Dr. MORRELL: No sir; these are definite chemical entities.

Mr. HOWARD: So it would not be possible for a physician to compound them; he would then have thalidomide and that is prohibited.

Dr. MORRELL: It is not easy to manufacture them. I do not think a doctor would manufacture them in his own office.

Mr. HOWARD: But in any event, if he did, it is prohibited.

Dr. MORRELL: Yes.

Mr. MITCHELL: I would like to direct a question to Dr. Morrell. The withdrawal of liefcort, or the suggestion that the doctor withdraw it would be for two reasons, I presume; in other words, (1) it was dangerous in respect of the dosage and (2) it had no medical use or had no curative action with respect to what he was using it for, and it would be for one of those two reasons that it would be removed.

Dr. MORRELL: No; we enforce the law and our enforcement action has to be taken on a breach of that law in some way or other. There is a section of the regulations, C.01.307, which governs the introduction of drugs for investigational uses. When we went to Dr. Liefmann's office, talked to him and saw his records, we found that he was not complying with some of the requirements of this section of the regulations. We asked him to do so and told him how he might do it. He agreed to do so. Subsequent visits indicated that he was not doing so and because he was then violating that section we told him he must no longer distribute the drug to anybody else for any purpose.

Mr. MITCHELL: Then, for the committee's edification, what was he violating insofar as that section is concerned.

Dr. MORRELL: The section requires that when he distributes his drug, it must be labelled for investigational use only—and I think there was a period in which he did not do that. He eventually corrected that. He was supposed to distribute it only to qualified investigators for the clinical trials. We questioned his qualified investigators. Finally he is required to collect investigators reports—that is detailed reports—of the investigation that these people had carried out. When we looked at these reports they were very unsatisfactory. They were either missing in some cases or they were far from complete in other cases. They were virtually only testimonials rather than detailed reports of a clinical trial. This was again pointed out to him and he said he would take the proper action. But, he did not, and then we told him he must not any longer distribute the drug.

Mr. MITCHELL: Then you were qualifying the active product yourself as being dangerous.

Dr. MORRELL: No.

Mr. MITCHELL: You were merely asking him to abide by the regulations which had nothing to do with the efficacy of the product according to the three ingredients in it.

Dr. MORRELL: No. Had a new drug submission eventually been made we would, of course, have looked very carefully at the evidence for hazards that might have developed. There is one thing I might go back and say; we did not see any reports of side effects in these reports from the clinical trials and looking at the composition of the drug, as we eventually knew it, we would expect some, and we did not see any. But had a new drug submission been made to us we would have looked for this and we would have also looked at the evidence he had for effectiveness. But none was ever made.

Mr. MITCHELL: No. You have not gone that far.

Dr. MORRELL: No.

Mr. MITCHELL: And even if he lived up to these regulations, which you say he did, and then the product was controlled to your satisfaction, you would or would not have any authority, shall I say, to qualify or investigate whether this was in use or not.

Dr. MORRELL: Well, if he makes claims for it we consider him as a manufacturer in this instance and not as a practicing physician. And if he made any claims that it was of value in the treatment of rheumatoid arthritis or arthritis we would have been very much interested and concerned with the information he supplied in his new drug submission to support this claim.

Mr. HARLEY: Mr. Chairman, I have a few more questions to ask Dr. Morrell on this matter. Is there any existing legislation through which your department can impose a time limit on an individual in respect of the investigational use of drugs? Is there a time within which an individual must submit a new drug submission?

My second point arises from an assumption on my part in respect of what you said. If Doctor Liefman came to the department and said he wanted again to do some investigational work on a drug, provided that he followed the regulations of your department, although he had perhaps just changed the dosage slightly, could he again distribute this drug to his patient?

Dr. MORRELL: There is certainly nothing in the law which states that he cannot.

As to the time limit, there is no time limit set down, and the time does vary greatly from a matter of a year to many years. The time in respect of LSD was many years.

Mr. HARLEY: Is there any time limit in respect of an interim report that a company would have to submit to you?

Dr. MORRELL: No, there is not.

Mr. HARLEY: Do you think it would be of assistance if there was a time limit in the regulations in respect of a drug being investigated, requiring a company to report every six months on its progress?

Dr. MORRELL: Such a regulation might be of assistance. We now have the authority to look at the company's records which the company has collected in respect of clinical trials and investigations. At the present time we can look at those records at any reasonable time, so that if we are suspicious of something we can see what has been going on or accomplished at any particular time.

Mr. HOWARD: Doctor Morrell, is Liefcort what one might call, as they are generally referred to, a combination drug which contains other drugs generally used for different purposes?

Dr. MORRELL: Liefcort is a brand name of a mixture of drugs. It is a mixture of three drugs, as far as we are aware, in some kind of medium or vehicle. It is a combined drug. The three drugs are well known.

Mr. HOWARD: Yes, but are they administered normally for different maladies?

Dr. MORRELL: Yes, they are individually administered for different things.

Mr. HOWARD: Undoubtedly you have seen the series of articles which have appeared in *Macleans* magazine this year with respect to the drug and so on. One of the articles dealt with this question of combination drugs, or the combining of drugs used for different purposes, resulting in a new therapeutic value. Do you now have within the food and drug directorate any facilities for testing the toxicity or efficacy of these drugs?

Dr. MORRELL: The efficacy, if I might refer to it first, can really only be obtained by clinical trials. We have no facilities whatsoever to carry out clinical trials.

Toxicity at times can be measured up to a certain point at least by tests on animals. We do have some facilities for testing toxicity on animals of various species. I want to point out that there are hundreds of new drug submissions sent to us every year. There are dozens of other materials such as food additives, pesticides and so on, submitted to us every year for some kind of examination or review. If we tested them all we would have to have a very, very large staff and a large colony of animals. Therefore, we feel, and I still think it is right, that the responsibility for testing the drug for these hazards and value rests with the manufacturer who is going to sell it. Our responsibility is to see that the manufacturer obeys the law when he makes his tests and puts his drug on the market.

Mr. HOWARD: Perhaps this is hypothetical, but suppose a manufacturer makes the required tests but the side effects or toxic effects which may result from a newly developed drug do not show up for some period of time, such as I gather was the case with thalidomide and other drugs which had a variety of side effects; and if you were to come to the conclusion that the toxic effects were extremely disastrous, what steps could you take to have the drug withdrawn from the market? Could you put it on schedule H?

Dr. MORRELL: At the present time we can put such a drug on schedule H.

Mr. HOWARD: Prior to now you could not do that?

Dr. MORRELL: No.

Mr. HOWARD: Do you have any authority to assess the efficacy of drugs as to whether one is better for some particular ailment than another, even though it is claimed to be?

Dr. MORRELL: We have an indirect authority that pertains to the labelling of drugs. One cannot label or advertise a drug falsely or in a manner that is likely to give an erroneous impression regarding its value. However, we have no other authority in respect of efficacy. I think that the efficacy of a drug can only be determined after very wide usage for a considerable time, I mean on millions of patients perhaps over a period of years by a large number of practitioners. So many drugs start out with a bang and somehow or other peter out. It is not possible to tell within a few months or within a year whether a drug is really going to be valuable in the long run. Then again its efficacy is a relative thing. It has to be determined whether it is effective on every patient to a certain degree or effective only on a few patients. This is all very difficult and I do not think that a government department should be the authority or the agency which says that this drug is of value and that drug is not of value. This can only be determined by the medical profession itself after a long usage of that drug.

Mr. HOWARD: There has been a tremendous increase, since the last few years anyhow, in the number of drugs that come on the market. Is this true? Do you anticipate that there will be a greater use made of schedule H in the Food and Drugs Act as a result of this?

Dr. MORRELL: It is always there, Mr. Howard, if it is needed. Personally I would think that schedule H should be used very sparingly.

Mr. HAIDASZ: Mr. Chairman, I am still not completely clear why the food and drugs directorate does not prohibit Dr. Liefmann from using liefcort on his patients.

Dr. MORRELL: The only answer I can give, unless someone else can think of another answer, is that he is not violating any section of the Food and Drugs Act and regulations. Unless we are going to get into some regulation that tells a doctor what he can prescribe, and in fact that regulates medical practice, I do not see how we can stop it. That is the only answer I can give you.

Mr. HAIDASZ: But you have already stated that the dose of estradiol is ten times above the therapeutic dose.

Dr. MORRELL: No, the usual dose.

Mr. HAIDASZ: Is that not unsafe?

Dr. MORRELL: Perhaps Dr. Murphy could answer that. He is a medical doctor.

Dr. J. B. MURPHY (*Chief Medical Officer, Food and Drug Directorate*): Well, Mr. Chairman, first of all I should point out that if a physician were treating a cancer patient with estradiol, he might well have to use doses of that drug well in excess of a recommended dose for, say, the treatment of dysmenorrhea, or something like this. With liefcort, all Dr. Liefmann did was to mix three drugs together. These were for the purpose of treating primarily rheumatoid arthritis. It was an experimental mixture and Dr. Liefmann deemed it advisable to have the drug mixtures in these particular doses. The fact that estradiol was ten times the usual recommended dose was known by Dr. Liefmann and in his judgment, I presume, he felt this dosage was necessary.

Mr. HAIDASZ: My question was whether in the judgement of the food and drugs directorate a dose ten times the therapeutic dose is acceptable in the treatment of rheumatoid arthritis.

Dr. MURPHY: This is a question which could only be answered after the patient has been treated.

Mr. HAIDASZ: There have been patients and there has been evidence of serious side effects.

Dr. MURPHY: But we also have evidence, on the basis of reports we have received both from physicians and testimonials from patients, that the drug combination was effective.

Mr. HAIDASZ: For what?

Dr. MURPHY: For the treatment of their arthritis.

Mr. HAIDASZ: But you have other evidence also that this drug has caused serious side effects.

Dr. MURPHY: We have heard of cases in which the use of the drug has caused some serious side effects to the patient.

Mr. HAIDASZ: You think this situation should continue?

Dr. MURPHY: I will only point out to you that many other drugs can cause serious side effects if misused either by the patient or if they are not given properly by the physician.

Dr. MORRELL: Mr. Chairman, the situation is not continuing in the sense that liefcort is being used by other physicians or that it is being distributed or manufactured in a commercial way. We are interested, under the Food and Drugs Act, in the commercial practice not in medical practice itself. If estradiol, which seems to be the ingredient of liefcort that is being spoken of just now, were given separately by a doctor in ten times the usual recommended therapeutic dose, I do not believe we would say that that doctor could not use estradiol in the future. It seems to me that this situation is analogous to that, Dr. Haidasz.

Mr. HAIDASZ: According to regulation C.01.307 we are also involved in the safety and dosage of drugs, and, as you said, liefcort or estradiol given in ten times the therapeutic dose is unsafe, therefore you are involved in safety.

Dr. MORRELL: I have not said that, Dr. Haidasz. It is possible that in some cases it would be quite safe. I have no evidence that on the whole you must stick only to the usual recommended dose of estradiol. I would think it should

be a doctor's judgement or a doctor's opinion as to what dose of estradiol he should give to a particular patient rather than have me tell him what dose he should give to a patient.

Mr. HAIDASZ: The whole problem is this, that you have ruled that thalidomide in certain cases is unsafe and therefore it must be banned, and yet liefcort is unsafe in certain cases and is not banned, it is not put on schedule H.

Dr. MORRELL: Liefcort in a sense is banned in that it is not commercially available. It is not now available for clinical trial; it is available only to Dr. Liefmann in his own practice. He buys the ingredients, he mixes them up—in what proportion at the moment I do not know—but there are many doctors in Canada and what they are giving to their patients I do not really know and I suppose it is not my business.

Mr. HARLEY: I have a question which does not deal with liefcort.

The CHAIRMAN: Any other questions on liefcort?

Mr. RYNARD: Dr. Morrell, I wanted to clarify this point. Is not this situation altogether different? Is Dr. Liefmann not now under disciplinary action of the Royal College of Physicians and Surgeons of the province of Quebec so that if he is doing anything wrong they will look after it?

Dr. MORRELL: There is such a thing as malpractice.

Mr. RYNARD: Therefore, this does not enter into the picture at all?

The second point is that therapeutic doses differ according to the condition the doctor is treating. There is no therapeutic level dose because it depends on the condition you treat.

Mr. BALDWIN: To go back to the point made by Dr. Haidasz, section C.01.307 applies to manufacturing and selling, but then, the response to Dr. Rynard indicates that this is in a different category, this is not a case of selling, to which C.01.307 applies.

Dr. MORRELL: That was the point I tried to make, sir.

Mr. HARLEY: Is everyone ready to leave the question of liefcort?

Mr. HOWARD: I have an indirect question.

Mr. HARLEY: I wonder if you could give us some idea of whether the rules of the food and drug directorate actually apply, and if so, how they apply to different vitamin preparations which are on the market in very profuse numbers? I am thinking particularly of the drugs which have come on the market in very large quantities under very strong tactics, such as "nutro-bio" and that type of thing.

Dr. MORRELL: You mean what can we do about this?

Mr. HARLEY: Yes. How do the rules of the food and drug directorate apply to food additives and diet additives?

Dr. MORRELL: There is a section in the food and drug regulations which deals with vitamins only—as you probably know—and this applies. There is a list of vitamins given which people may represent as being vitamins and the amounts which are permitted in various preparations are listed; if you are going to sell a preparation as a vitamin supplement, you may not have in the vitamin preparation more than a given amount of each vitamin, and actually that is all listed.

If you are going to sell a vitamin preparation for therapeutic use, in the treatment of a deficiency disease, you must go higher in your vitamin content in the preparation, and it is lawful, but you must label it for therapeutic use only. You do not advertise it to the general public at all. This is also listed. In other words, there is a level beyond which the product—if it says that it contains vitamins exceeding that level—must be labelled for therapeutic use only and not advertised to the general public.

The claims which can be made for each of the vitamins are specified in these regulations.

Now, in respect of enforcement measures we pick up samples; usually they are picked up as samples from products on the market, and we analyze them for their vitamin content. We also look at the label to see if it meets the requirements of the regulations, and we would look at the claims made, whether they be in advertising or on the label, to see that they do not exceed those laid down in the regulations.

These requirements apply to all vitamin products sold in Canada whether by unusual means—such as you mentioned—or sold in pharmacies. We try to apply them across the board. Does that answer your question?

Mr. MITCHELL: The date is necessary on certain vitamins, is that correct?

Dr. MORRELL: We have an indirect date on the vitamins, in as much as the batch number indicates the date of manufacture according to a code which gives our inspector, the pharmacist and the manufacturer, of course, an indication of the date on which it was made. Therefore those who are selling and dealing with it—and our own people—are able to tell when the product has been on the market for perhaps too long.

Mr. HARLEY: I would like to return and ask a question in reference to what we were talking about a few minutes ago. It was my understanding that the drug I mentioned, and similar ones like it, would actually come within the ruling of the food and drug directorate because they were labelled as something else, and not vitamins.

Dr. MORRELL: That certainly came within the purview of the Food and Drugs Act, and of the authority of the regulations; and we did go further, as a matter of fact. I think the members of the firm promoting it came to see us about their advertising and we corrected it and brought it down to what we thought was in line with the requirements of the regulations. The product itself was analyzed and the packages in which they came were examined, and in so far as we were able to ascertain, it was sold in a legal manner. We of course were not able to be present at the door when the salesman was there, so we do not know exactly what he said. But all printed advertising was within the requirements of our law.

Mr. HOWARD: Sometime in the later part of 1960 the directorate submitted or prepared some draft regulations with respect to drugs which were to have been submitted to the minister after they had been circulated to the drug manufacturing industry; and there was some discussion in the house about it around that time. Could you tell me what happened to those proposed regulations?

Dr. MORRELL: Yes.

Mr. HOWARD: Perhaps this matter was dealt with when I was unable to be present, at a previous meeting.

Dr. MORRELL: What you refer to as regulations are trade information letters; they were not regulations at all. There was an information letter containing a proposed draft of regulations which we thought would be useful and perhaps necessary in controlling the manufacturing controls in relation to the production of pharmaceuticals and other drugs. The proposals were sent out to the industry and we had comments from various parts of the industry, and we had meetings with them. We remodified them to some extent and we sent them around again, and we ourselves had a lot of discussion among ourselves and so time passed. Last fall I believe they were submitted to the minister and there has been some discussion about them since. I think they are before him now.

Mr. HOWARD: One of the things which intrigued me about it is this: I could not get them in the house by motion; so we had to try another way to get them. It says, as proposed in C.01.014—is that the way you designate these clauses?

Dr. MORRELL: Yes.

Mr. HOWARD: It reads as follows:

> C.01.014. No manufacturer shall sell a drug unless the drug has been manufactured and tested under conditions that are suitable to ensure that the drug will not be unsafe for use.
>
> C.01.014. For the purposes of C.01.014 the conditions that are suitable to ensure that a drug will not be unsafe for use shall include:
>
> (i) a system of control that will permit a complete and rapid recall of any lot or batch of a drug from the market when such is found to be unsatisfactory or dangerous.
>
> (j) the maintenance, in a form, manner and content satisfactory to the director, of records showing:
>
> (vi) the measures taken to ensure the recall from the market of unsatisfactory or dangerous lots or batches of drugs.

The CHAIRMAN: Dr. Morrell did say yesterday in answer to questions from Dr. Horner and Dr. Orlikow that there was a certain section which was intended to tighten up this situation. I thought I should draw that to your attention, Mr. Howard.

Mr. HOWARD: Yes, certainly. Perhaps this is something you would not care to answer, Dr. Morrell?

Dr. MORRELL: No, no.

Mr. HOWARD: Are these provisions, as attached to your trade information letter of December 28, in the proposed regulations which you submitted to the minister last fall?

Dr. MORRELL: They are still there, yes.

Mr. BALDWIN: I would like to deal with another subject which is somewhat related to what we have been discussing so far. Under the Broadcasting Act I understand that indirectly certain responsibility comes on your department in that before there can be commercial advertising permitted of drugs the advertisement must be approved by your department. Dealing with the procedure in that regard—and in answering you might give us some idea of what is done—do you feel, in the procedure followed now, that the material submitted to you by the various advertisers is satisfactory so that you are capable of delivering the opinion you are called upon to give?

Dr. MORRELL: Mr. Chairman, as Mr. Baldwin has said, in the regulations under the Broadcasting Act there is this requirement that all commercials for T.V. and radio must be submitted to the Department of National Health and Welfare for approval—and the word "approve" is used—before they are put on the air. There is an arrangement now under which T.V. and radio commercials are sent to us routinely. I think there are 30 to 35,000 per year which come to us. These are examined by a group of persons who are technically qualified in the inspection services of the headquarters to see that they comply with the requirements of the Food and Drugs Act in respect of advertising. In fact, the section reads to the effect that no person shall advertise any product—

Mr. BALDWIN: Sections 5 and 9.

Dr. MORRELL: You are right. There is a good deal of work necessary on many of them. A blue pencil is used quite frequently. When we are finished with it the script is returned to the broadcasting officer who deals with these and then I think of course they are looked at from their own point of view, too. I

think, however, that the arrangements are quite satisfactory in so far as we are concerned now, and I think we have been able to deal with them quite well. That is my opinion, at least.

Mr. BALDWIN: You feel that you have an adequate staff to deal with the quantum of 35,000 in a year?

Dr. MORRELL: Well, it is pretty fast work.

Mr. NICHOLSON: I would like to follow up what Mr. Baldwin has had to say about this matter. How closely does your branch work with your opposite numbers in the United States? I am thinking now of the larger cities like Montreal, Toronto, Hamilton, Windsor and Vancouver, all of which have American T.V. and radio stations coming in to them. Speaking for myself, so far as Vancouver is concerned, we get far more advertising from United States stations telling us the wonderful properties of these drugs that come on the market. You must have a working arrangement with the United States on that. Do they have similar provisions? How do you work on this as between the respective branches of government?

Dr. MORRELL: We have not been able to exercise any authority over advertising that originates in the United States. I might add that this is also true of printed advertising which comes in here from the United States. The food and drug administration in Washington does not have authority over advertising in the sense that the food and drug directorate in Canada has. In the United States the control of advertising is exercised by the federal trade commission in Washington. I have visited the federal trade commission and have spoken with them about the problems which arise because of the differences in our laws; but they have not been able to suggest anything which would be particularly helpful to us. So, I am afraid we are faced with this difference between the advertising originating in the two countries. Frankly, I do not know what to do about it.

Mr. HORNER (*Jasper-Edson*): I would like to question Dr. Morrell in respect of quality control. First of all, do you think this is a government responsibility or a responsibility of the manufacturer.

Dr. MORRELL: I think quality control is a responsibility of the manufacturer firstly, positively and very strongly. Then, secondly, I think the government has a part to play in seeing that the manufacturer does have and does exercise adequate and suitable quality control over his products.

Mr. HORNER (*Jasper-Edson*): I notice in the annual report you say that your recommendations in respect of the new regulations will help you do this; that is, help you to have some supervision over quality control.

Dr. MORRELL: Yes, indeed; I am sure they will.

Mr. HORNER (*Jasper-Edson*): Which you do not have now?

Dr. MORRELL: Not in nearly the same degree; they are not spelled out in the detail they are spelled out in the proposed regulations.

Mr. HORNER (*Jasper-Edson*): I am thinking primarily of the important antibiotics going out under their generic names. Will this have an effect on these?

Dr. MORRELL: I think it will, yes.

Mr. HARLEY: First of all, has the medical profession, as a profession and not as an individual, ever asked the food and drug directorate to remove a drug from the market?

Dr. MORRELL: No.

Mr. HARLEY: Mr. Chairman, I wonder whether this committee would consider a five minute recess to give Dr. Morrell a short respite from his questioning?

The CHAIRMAN: Is the committee in agreement with that request?

Agreed.

The CHAIRMAN: We will resume at five minutes to 11 sharp.

—Recess.

—Upon resuming:

The CHAIRMAN: Order, gentlemen. We will commence with Dr. Harley.

Mr. HARLEY: Mr. Chairman, I was wondering if perhaps we could switch the questioning and ask, through you, some questions of Mr. Hammond. I am thinking particularly of the control of drugs and I would like to ask him if he can tell us whether there is much of a problem these days in connection with the control of narcotic and controlled drugs.

Mr. R. C. HAMMOND (*Chief of the Narcotic Control Division, Department of National Health and Welfare*): Mr. Chairman, we do have problems in respect of both narcotics and controlled drugs. In so far as narcotics are concerned, the material that is being distributed in Canada for medical use causes few if any problems in the illicit traffic because of our system of control and the co-operation which is afforded to the department by those entrusted with supplies.

A somewhat different situation exists in relation to the controlled drugs (the barbiturates and the amphetamines); in other words the depressants and stimulants. The material causing the problem up until recently was supplies that were being diverted from that intended for medical use.

To recapitulate, the narcotic material causing problems in Canada is heroin which is being smuggled into the country, and in so far as the depressants and stimulants are concerned, the material which has been subject to abuse is medical supplies being diverted.

Subsequent to September, 1961, when the legislation in reference to controlled drugs was brought into force, a licensing system was provided over distributors and manufacturers and in addition controls in the form of records at the retail pharmacy level. Since that time there has been a marked improvement in so far as controlled drugs are concerned.

Mr. HARLEY: This question would probably be a better one to pose to the R.C.M.P. However, have you any idea of the amount of illegal trafficking going on in connection with these two groups and, as we have been talking about the safety of drugs, have you any idea of the number of fatalities recorded in Canada as a result of the illegal use of these materials?

Mr. HAMMOND: I cannot comment on that. We are endeavouring to maintain statistics in connection with fatalities. We know in the city of Vancouver for example, within the last three years, there has been quite a noticeable increase in the number of fatalities attributed to the use of barbiturates. I would not even venture to give a figure at the moment, but I think in 1962 the total number of fatalities which occurred from January 1 to August 1 of that year almost equalled or exceeded the number of fatalities in the previous year.

Mr. HARLEY: Would that figure cover fatalities from overdosage, or would it include suicides?

Mr. HAMMOND: This figure I believe would be separate from the figure in respect of suicidal deaths.

Mr. NICHOLSON: Following up that line of thought, is it not a fact that many of these fatalities result because people in a confused state of mind mix different things without knowing the right proportions? Have not the verdicts of coroners inquiries disclosed that fact in Vancouver?

Mr. HAMMOND: Many of these fatalities result from the combination of alcohol and barbiturates.

Mr. NICHOLSON: I understand these individuals take goof balls with alcohol in an attempt to get the biggest kick without there being any medical knowledge involved.

I am not sure, Mr. Chairman, whether the question I intend to ask should be directed to Doctor Morrell or not. Has anyone on your staff, Doctor Morrell, made a study of the work that has been going on in Britain where they have these clinics supplying narcotics to drug addicts? I have read a great deal about this program in the newspapers but I am not sure of the accuracy of these reports. Has anyone made a study of whether or not that program is in fact curtailing the use of narcotics or preventing associated crimes?

The CHAIRMAN: I might just say that I do not intend in any way to restrict this committee but my view is that we are straying a little far from the aspect of safety in regard to drugs in Canada. I may be wrong in that view and I hope members of this committee will give me their views in this respect.

I think Doctor Cameron will have something to say in regard to that question.

Dr. CAMERON: Mr. Chairman, we are endeavouring to follow the work being done in Britain and we certainly are in consultation with medical groups and others in this country with a view to finding improved methods of dealing with confirmed addicts. I do not think the information we have from Britain so far makes it possible to draw any hard or fast conclusions about the success of the work which they are doing there.

Mr. NICHOLSON: I do not wish to pursue this matter to any great length, but a great deal of attention has been directed toward this program through newspapers and other news media. I am not sure of the accuracy of the press and other reports in this regard. Is it possible, or do you know, Doctor Cameron, for an addict in Britain to get a fix, as they refer to it, quite readily?

Dr. CAMERON: Are you referring to Canada?

Mr. NICHOLSON: No, I directed my question in respect of England. Are the newspaper articles which indicate this availability of drugs to addicts exaggerated?

Dr. CAMERON: I think the position there is that if a duly qualified medical person wishes to undertake the treatment of an addict it is perfectly legitimate for him to do so. Here and there you will find medical people who take this type of treatment upon themselves.

If such a doctor in the course of that treatment decides that it is reasonable to give an addict a dose of a drug it is perfectly legitimate.

The aspect of this which is contrary to the law here, and I imagine it is also in Britain, although I cannot say for certain, is the provision of drugs for the purpose of peddling them. If the drug is being given for treatment and honestly administered by a physician in the belief that he is doing this properly, then it is not against the law and we would not interfere with such a practice at all.

It is perfectly evident to us all, and I might even say glaringly evident, that we need much better methods of dealing with drug addiction than we have at the present time. We do not feel that we are really coping with this problem at all. We are trying to suppress the illegal trafficking in drugs, but the progress in the direction of a reasonable and effective treatment of a drug addict is very very slow and discouraging.

Mr. HARLEY: Mr. Chairman, I should like to direct my line of questioning to that aspect of our scope of the terms of reference. I am referring to controlled drugs and the associated enforcement in this regard.

In view of the results attained by the inclusion of amphetamines and phenobarbs in the controlled schedule, do you feel that it would be of assistance to you if this new family of tranquilizers was also included in the controlled schedules? If your answer is in the affirmative, then I should like to ask how much additional work and change such a step would mean to your department in terms of staff and money.

Dr. MORRELL: Mr. Chairman, we are of course watching the sale of drugs other than those which are on schedule G. The purpose of schedule G, as I understand it, is to stamp out the illegal trafficking on the streets by pedlars to those individuals wishing to buy them in dance halls, or wherever they do buy them. As far as I know that was the sole purpose of the amendment to the act and the regulations involving the enforcement of schedule G. If we find that there is evidence that trafficking in drugs other than those under schedule G, I would feel we will have to make a recommendation to the minister that such other drugs be added to the schedule.

I cannot say at this time whether this illegal sale is imminent or very likely in the near future, but it certainly is a possibility which we have in mind.

Secondly, and perhaps Mr. Hammond could say a word or two in this regard, having had years of experience in the enforcement of the Narcotic Control Act, the addition of the extra work required by the enforcement of schedule G has been very considerable. The reason for this is that of the much wider use. Mr. Hammond can correct me if I am wrong, but I feel there are more dealers and more products in this regard and therefore a great deal more work in connection with the enforcement of schedule G than perhaps there is in connection with the Narcotic Control Act. Any addition to schedule G of a group of drugs such as all of the tranquilizers would of necessity require a very considerable increase in the work of enforcement. I do not think such an addition would be justified unless there is evidence of significant trafficking in these particular drugs. This is the attitude we are now adopting.

Have I answered your question?

Mr. HARLEY: I wanted to ask Mr. Hammond whether he would like to comment on the increase in the work of enforcement if such drugs were included in schedule G.

Mr. HAMMOND: Mr. Chairman, as Doctor Morrell pointed out, controlled drugs are used much more extensively, as Doctor Harley will realize, than narcotics, and the increase in the work involved to establish control is considerable.

We have roughly 160 odd firms licensed to deal in narcotics and there are approximately 320 odd firms licensed to deal in controlled drugs. While I think that controls in themselves are essential, other factors are equally important in preventing abuse of these drugs.

The CHAIRMAN: At the last meeting several members of the committee asked me if I would get Mr. Curran to explain the federal-provincial responsibility with regard to licensing in a full way, if possible. I wonder whether it is the wish of the committee now that Mr. Curran make his statement on that.

Mr. NICHOLSON: How long is it likely to take, Mr. Chairman?

Mr. R. E. CURRAN (*Legal Advisor, Food and Drugs Directorate*): Mr. Chairman, it should not take too long. It depends on the number of questions that will be asked.

The CHAIRMAN: Was there some reason, Mr. Nicholson? Is there another meeting you wish to attend?

Mr. NICHOLSON: Yes. The Liberal contingent here has a problem.

The CHAIRMAN: Mr. Curran, if you could make your statement between now and 11.30, we will then reserve the questions until the next meeting. Would that be all right?

Mr. NICHOLSON: Yes.

Mr. CURRAN: Mr. Chairman, firstly, I am glad to have the opportunity to clarify a position which is not always clear even to lawyers, and also I hope I will be forgiven if I do not make this thing as clear as I might to people who are not lawyers.

The Food and Drugs Act, as I mentioned at the last meeting, is on the basis of criminal law, and under the authority of criminal law there is no power to license a trade or profession generally. Now, I wish to distinguish between licensing particular products which are manufactured by the trade and licensing a trade to carry on generally its operations. If you look at sections 12 and 13 of the act you will see this distinction.

The CHAIRMAN: What page?

Mr. CURRAN: Page 3 of the act. You will see in sections 12 and 13 that no person shall sell any drug described in schedules C, D or E unless the minister has, in prescribed form and manner, indicated that the premises in which the drug is manufactured and the process and conditions of manufacture therein are suitable to ensure that the drug will not be unsafe for use. Following along from that, if you look at pages 91 and 100 of the regulations you will see that regulations have been made to implement the provisions of the two sections to which I referred. The first of them is on page 91 and it deals with what are called "schedule C drugs". On page 100 you will see reference to drugs which are on schedule D. The licensing authority here is very strictly limited to the manufacturing process and the conditions of manufacture to ensure that the drug is not unsafe for use. These are the criteria which form the basis of licensing in both of these areas.

Some reference has been made to licensing of controlled drugs. This is pursuant to a special part of the act which is part III and which was added a year ago. I am not going to get into the question of narcotics which involves separate consideration but nevertheless is much on the same basis. So we have under the authority of sections 12 and 13 and under the authority of part III provided for a form of licensing in relation to particular substances. This must be distinguished from the licensing of a trade in general to carry on its business. Here the licence is limited to particular products, and obviously based upon some reason to subject a drug to this form of licence. In the case of the drugs in schedules C, D, and E, I think the reason is given in referring to the conditions of manufacture being suitable to ensure that the drug will not be unsafe for use. Even though a licence is given, it does not mean that the drug does not otherwise have to conform to the requirements of the law. Broadly, every drug which is sold in this country, either manufactured here or brought in, must conform to two provisions of the act amongst others: one is that the drug must meet the standard under which it is manufactured and the standard must be identified on the label, and the other is that the drug may not be deceptively advertised or sold. These are the general overriding conditions which apply to all drugs including those for which a licence is granted.

Now, it has been suggested from time to time that we should have a provision that no person shall manufacture any drug unless he has a licence. Such a provision in my view would certainly be at least arguable as to validity, subject of course to any different views held by the lawyers on this committee as to whether they feel this would be a valid exercise of parliamentary authority. I think, under the basis of the Food and Drugs Act, it would

be a very dubious provision and easily could be challenged in court and imperil the very broad and good administration which has been developed. So we have been very careful to limit our licensing authority to those drugs which pose special problems either in health fields or perhaps in the broad field of fraud—but particularly in the health field—where the conditions of manufacture have unusual features and where safety of a drug as related to manufacture may not be readily detremined even on analyses.

There are many drugs which on analysis of the end product might not reflect certain essential conditions of manufacture, and so it is necessary, in relation to those drugs, to ensure that the conditions of manufacture are adequate for the purpose, and to ensure that the drug will not be unsafe for use.

That, broadly, is the basis on which we have developed a form of licensing. You will see that even in the act itself we are very careful in sections 12 and 13 not to use the word "licensing". We talk about the prescribed form and manner of the ministers indication of approval which in effect is a form of licensing. We have used the word "licence" in controlled drugs, which involves separate considerations.

Now, at the provincial level it would be appropriate, I think, under the authority which is contained in section 92 of the British North America Act, for a province under the property and civil rights provision to insist on the form of licensing of any manufacturer carrying on business in the province. I am not prepared to say to what extent the provinces have got into the form of licensing but certainly it would be of very dubious validity if the federal government, under the authority of the Food and Drugs Act purported to license every manufacturer for a drug. So I want to make it abundantly clear that we are distinguishing between the general authority to license a trade or business, which in my view is beyond the competence of parliament, and the authority to license a manufacturer in relation to a particular product which can be potentially harmful.

Mr. MITCHELL: May I ask Mr. Curran a question? Speaking provincially, would this be under the provincial department of health or under the pharmacy act or something of that nature?

Mr. CURRAN: It could be under any form of legislation the province wished to devise. It could be under the factories act which would require a form of licensing, or under the pharmacy law or under the department of health of a province. Where a province puts the authority is its own decision.

As I said a moment ago, I am not prepared to say to what extent the provinces have entered into this field. I think the field is one in which the provinces have not intervened even though they might do so. There are many factors which would need to be considered by a provincial authority in licensing a manufacturer and particularly one which was carrying on business in many parts of Canada as well as perhaps internationally. This poses a separate area and the area I have broadly attempted to explain is the licensing of certain products under the Food and Drugs Act. I might add that the schedules in question can be amended by adding anything to the schedules or deleting anything therefrom in the interest of health.

I have attempted to explain the rather unusual situation which arises when we talk about licensing a product in one context, while in the other context we say that we have no authority to license a trade. If I have made clear to you the subtle distinction between licensing a product and licensing the manufacturer at large, I am glad. If not, I would be happy to try again. Does what I have said generally cover the situation?

The CHAIRMAN: I think so. We have only four minutes, gentlemen.

Mr. NICHOLSON: While Mr. Curran is here, there are a couple of points concerning the work of this committee which disturb me. First of all, I refer to section 13 of the Food and Drugs Act which reads as follows:

> 13. No person shall sell any drug described in schedule E unless the minister has, in prescribed form and manner, indicated that the batch from which the drug was taken is not unsafe for use.

Does that mean that every new batch of a drug has to be approved by the minister—or by his representative?

Mr. CURRAN: Yes. Broadly speaking, with respect to the drugs in schedule E, a sample test is made from each batch.

Mr. NICHOLSON: You mean from every individual batch?

Mr. CURRAN: Every batch, that is right. Before the drug is released for sale, there must be clearance given by Dr. Morrell that the drug has met the particular condition.

The CHAIRMAN: That only applies to the drugs mentioned in schedule E?

Mr. NICHOLSON: I know, but schedule E is very comprehensive. Just how are the tests made? Is it done by means of a spot check?

Dr. MORRELL: You will notice the drugs on schedule E are mentioned at page 10 of the act.

Mr. NICHOLSON: There are 6 classifications given in schedule E, and I notice "sensitivity discs and tablets".

Dr. MORRELL: Sensitivity discs and tablets are those paper discs or tablets which contain various antibiotics and which are used to test the sensitivity of bacteria or effectiveness of certain antibiotics against certain bacteria which may be affecting the patient. Each one of these is tested prior to distribution. This involves, of course, quite a lot of work as you will imagine.

Mr. NICHOLSON: It is not done by means of spot tests? There is an actual detailed test made of each batch?

Dr. MORRELL: That is right.

Mr. HARLEY: There would not be very much volume in the actual amount in the case of most of these drugs?

Dr. MORRELL: When I started to work in the laboratory, these were quite important. But with the introduction of antibiotics such as penicillin, this has made them of rather minor therapeutic use.

Mr. NICHOLSON: My next question is prompted by section 14 subsection 2 "distribution of samples prohibited".

> 14. (1) No person shall distribute or cause to be distributed any drug as a sample.
>
> (2) Subsection (1) does not apply to the distribution of samples of drugs by mail or otherwise to physicians, dentists or veterinary surgeons or to the distribution of drugs, other than those mentioned in schedule F, to registered pharmacists for individual redistribution to adults only or to a distributor in compliance with individual requests.

The distribution of samples is done on a large scale to doctors, and subsection 2 of section F is so wide, that I wonder why samples are not distributed to pediatricians, for instance, and why they are limited for distribution to adults only?

Dr. MORRELL: That has been amended, as you know by bill C-3, and it is no longer the law.

Mr. CURRAN: There is a new section 14 in the amending act.

Mr. NICHOLSON: Perhaps I had better get it and study it before I pursue this.

Mr. HARLEY: I believe it includes all branches and pediatricians. Certainly pediatricians do get samples.

The CHAIRMAN: It is just about 11.30, and before we adjourn, may I say that on Tuesday next, February 5, at 9.30, a special committee of the Royal College of Physicians and Surgeons will be here. I hope you will have a chance to look at their brief over the weekend. I also hope that this presentation and the questioning of the people who are going to be here might be finished on Tuesday, for certain reasons. However, if it cannot be done, then that is that. But we are thinking of sitting from 9.30 to 12.30, and after the orders of the day until 5.30 in the hope that in those 5 hours we might be able to get this matter cleaned up.

Mr. MITCHELL: We will be coming back to the witnesses who are here now?

The CHAIRMAN: Oh yes, the witnesses of the department are available.

Mr. MITCHELL: You are only suggesting that the out-of-towners be given a hearing next week.

The CHAIRMAN: I think it is only fair when any witnesses are brought here from away that we give them a specific time so that they will not be here a week or two. The men coming are very busy, so if we could confine our examination to the witnesses, that would relieve two or three members until next week and we could get it done expeditiously.

In respect of our proposed trip to Montreal the first of the week I shall be asking the house for permission. We shall start on February 14, a Thursday. The train leaves the Ottawa station at 7.55 in the morning. I hope there is no objection to that.

Mr. BALDWIN: Would it be possible for Dr. Cameron or Dr. Morrell to make available to us the 1961 amendments, and the amendments for this year to supplement the consolidated statutes that we now have?

The CHAIRMAN: Yes, Dr. Morrell will do that.

The other point I wish to bring up is that the Canadian Pharmaceutical Manufacturers Association will be here on March 5th and we have arranged for it. They are bringing a complete presentation and also specialists in the fields of pharmacology and chemistry, that is, from the industries they are involved with, and they are preparing papers for us in each of the sections involved in the presentation. So we will have a very comprehensive hearing. The reason we have left it until March 5 is to give them ample time to have all these things prepared, for it will be done in great detail.

Mr. HARLEY: Could they provide the material to us before they arrive?

The CHAIRMAN: You mean if we could get their brief beforehand; but there will be a general brief from their association, and each of the specialists in the fields will give a supplementary paper which I think he would want to give personally rather than to have a written statement given to the committee beforehand. But so far as the over-all production of the brief is concerned, there will be ample time for it.

Mr. NICHOLSON: I think we should get it as far in advance as possible.

The CHAIRMAN: I shall ask them to give it to us in advance. I hope there will be sufficient length of time.

Mr. NICHOLSON: I hope you will suggest a few days.

The CHAIRMAN: Perhaps we had better discuss this right now. It is my view that if a witness is coming to this committee he should be required to send us a

written statement beforehand. But in general practice if we bring a pharmacologist, let us say, from the University of British Columbia, to examine him on something specific, I do not think he should be required to file with this committee the evidence of what he is going to say. However, I think that with associations, at least, they should give us an outline of what they are going to do specifically, but I do not think they could be forced by this committee to give a complete documentation of what specialists they intend to bring in are going to deal with. Is that in accordance with the wishes of the committee? Is there any further business?

Mr. HARLEY: Is it the intention of the committee to sit this afternoon to try to finish our questioning of Dr. Morrell?

The CHAIRMAN: It is my view that there will be other business on our mind that we might all want to think about this afternoon, and that we might wait until 9:30 on Tuesday morning next.

OFFICIAL REPORT OF PROCEEDINGS AND EVIDENCE

This edition of the Minutes of Proceedings and Evidence contains the text of Evidence in the language in which it was given, and a translation in English of the French texts printed in the Evidence.

HOUSE OF COMMONS

First Session—Twenty-fifth Parliament

1962-1963

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. R. M. T. McDONALD

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 4

TUESDAY, FEBRUARY 5, 1963

WITNESSES:

Dr. F. S. Brien, B.A., M.B., F.R.C.P.(Lond), F.R.C.P.(Canada), F.A.C.P., Professor of Medicine and Head of the Department, University of Western Ontario, London (Ont.); Dr. R. Roger Dufresne, B.A.M.D., F.R.C.P. (Canada), Director, Department of Medicine, University of Montreal, Montreal (Que.); Dr. E. A. Sellers, M.D., Ph.D., Professor of Pharmacology and Head of the Department, University of Toronto, Toronto, (Ont.); Dr. G. D. W. Cameron, Deputy Minister of National Health; Dr. C. A. Morrell, Director of the Food and Drug Directorate.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1963

28336-6—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. R. M. T. McDonald

Vice-Chairman: Mr. Georges Valade

and Messrs.

Baldwin	Harley	Martin (*Essex East*)
Enns	Horner (*Jasper-Edson*)	Mitchell
Fairweather	Howard	Nicholson
Haidasz	Marcoux	Patterson
		Rynard—15

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

MINUTES OF PROCEEDINGS

TUESDAY, February 5, 1963.
(5)

The Special Committee on Food and Drugs met at 10.10 a.m. this day, the Chairman Mr. R. M. T. McDonald, presiding.

Members present: Messrs. Baldwin, Fairweather, Haidasz, Harley, Marcoux, McDonald (*Hamilton South*), Mitchell, Nicholson, Rynard, and Valade—(10).

In attendance: Dr. F. S. Brien, Professor of Medicine, and Head of the Department, University of Western Ontario, London, Ontario; Dr. E. A. Sellers, Professor of Pharmacology, Head of the Department, University of Toronto, Toronto, Ontario; Dr. R. Roger Dufresne, Director, Department of Medicine, University of Montreal, Montreal, Quebec; *from the Department of National Health and Welfare:* Dr. G. D. W. Cameron, Deputy Minister of National Health; Mr. R. E. Curran, Legal Adviser; Mr. Eric Preston, Director of Personnel; Mr. B. Hazelton, Personnel Administrator for Food and Drugs; Mr. D. H. Dunsmuir, Executive Assistant to the Minister; Dr. C. A. Morrell, Director of the Food and Drug Directorate.

The Chairman observed the presence of a quorum. He introduced the three members of the Special Committee on New Drugs appointed by The Royal College of Physicians and Surgeons of Canada at the request of the Minister of National Health and Welfare, namely: Dr. Brien, Dr. Sellers and Dr. Dufresne, and invited the Chairman of the said committee to make a statement based on the contents of their report.

Dr. Brien emphasized the working conditions of the Food and Drug Directorate and the need for a method to deal with drugs that have been used for many years. He also dealt with the recommendation pertaining to the establishment of a "Working" standing drug committee.

The Chairman thanked him and the other two members of the Special Committee on New Drugs for the work they have done during seven months to prepare this Report.

Dr. Brien, assisted by Dr. Dufresne, Dr. Sellers and Dr. Morrell answered questions, more particularly Need for Expansion of the Food and Drug Directorate, and Clinical Trials in Canada.

At 12.15 p.m. the Committee adjourned until 3.30 p.m.

AFTERNOON SITTING
(6)

The Committee reconvened at 4.15 p.m. and continued its examination of the members of the Special Committee on New Drugs appointed by The Royal College of Physicians and Surgeons of Canada.

Members present: Messrs. Baldwin, Enns, Fairweather, Haidasz, Harley, Marcoux, McDonald (*Hamilton South*), Mitchell, Nicholson, Rynard, Valade—(11).

28336-6—1½

In attendance: Same as at morning sitting.

At the request of the Chairman, the Committee agreed to hear Dr. Sellers first.

Dr. Sellers made a short statement on Sections 4 and 5 of the Report dealing with Concepts of New Drug Control and Present Procedures of the Department with respect to New Drugs. Dr. Cameron added an explanation about training of departmental staff. Dr. Sellers, Dr. Brien and Dr. Dufresne were jointly questioned. Dr. Sellers was permitted to leave.

On Section 10, Consideration of the Division of the Food and Drug Directorate into Food and Drug Sections, Dr. Brien, Dr. Morrell and Dr. Dufresne answered questions asked by Members.

Sections 12 and 13, Summary of Recommendations and Conclusion were considered.

Before concluding the discussions, the Chairman thanked Dr. Brien, Dr. Sellers and Dr. Dufresne for appearing before the Committee and for the information they had given. He expressed his regret that Committee proceedings had appeared to be rushed and were delayed in starting. These circumstances, however, were beyond the control of the Committee.

On motion of Mr. Mitchell, seconded by Mr. Rynard,

Resolved,—That the Report of the Special Committee on New Drugs appointed by The Royal College of Physicians and Surgeons of Canada at the request of the Minister of National Health and Welfare be printed as an appendix to the Minutes of Proceedings and Evidence of today's sitting. (See appendix "A").

At 5.50 p.m. the Committee adjourned until Thursday, February 7, at 9.30 a.m.

Gabrielle Savard,
Clerk of the Committee.

EVIDENCE

TUESDAY, February 5, 1963.

The CHAIRMAN: Gentlemen, we have a quorum. Before we get to today's proceedings I would like to check just one thing with the committee. The clerk of the committee sent around a note about a proposed trip to Montreal next week. I wonder if those who are going would inform her before tonight so that we can make definite arrangements.

We have with us today the special committee of the Royal College of Physicians and Surgeons pertaining to the new drug situation. Dr. F. S. Brien, professor of medicine and head of the department of the University of Western Ontario and chairman of the special committee of the Royal College is on my right. Dr. Roger Dufresne, director of the department of medicine, University of Montreal, is on the right of Dr. Brien, and Dr. E. A. Sellers, professor of pharmacology, head of the department of the University of Toronto is on Dr. Dufresne's right.

It was thought that the chairman of this committee would make a statement, and then this committee could ask questions on the general statement, but, for continuity, it was thought that in the context of the proceedings of the Royal College we should keep to specific questions so that we would have continuity. If that is in accordance with the views of the committee I think we will now call on Dr. Brien to make his initial statement.

Dr. F. S. BRIEN (*Professor of Medicine and head of the department, University of Western Ontario and chairman of the special committee*):

Mr. Chairman, I presume that you are all quite familiar with the contents of this report. There are just a couple of areas that I would like to emphasize. In the first place, it is perfectly obvious to us as a committee that the food and drug directorate is working under conditions that, to say the least, are infinitely more difficult than it can cope with with its present staff. Therefore, we have pointed this out and we have recommended to the minister that steps be taken to increase the membership of the directorate particularly in the higher echelons. As you already know, considerably more than 50 per cent of the time and energy of many of the directorate is expended on food and food additives as contrasted with drugs, and we have given various reasons for the need for increased staff.

The second point I would like to make is that as we have proceeded through the study which actually has encompassed about seven months, it has become quite obvious to us that there is a need for a consideration not only of our methods for dealing with drugs that may properly be termed new within the framework of the act but also with respect to any old ones, ones that have been used for many years. This, in particular I think, is important with respect to, firstly, children, and secondly, pregnant women. The hazards and the effects of drug dosage that have been hitherto unsuspected have become increasingly apparent over the last few years especially. This was one of the reasons why the other recommendation which we consider to be most important was, further setting up, either from the presently existent Canadian drug advisory committee or from other sources, or partly from it and partly from other sources, what we chose to call a standing drug committee. You will notice that we put "working" before the capitalized words "standing drug committee". I am

perfectly sure, and I think I have the concurrence of my colleagues here to my right, when I say that if this committee is going to be any good it will require the same kind of effort that the three of us have put into this report and all that has gone before it.

I am sure that some sort of a committee such as that can grapple with problems not only as they arise but also with the ones we have dug out in this list of appendices which totals 48—and I have another one which I received last week, which I will submit as a latecomer and which I think you will find very interesting. In it, and particularly in appendix 48, are brought together the subjects that we as a group felt required the most pressing or the most urgent study. We felt that this committee should be a continuing one and that it should not be a static group. We did not specify the number but we felt it should be a relatively small one in which most, but not necessarily all, of the members should be physicians, and that they should be appointed with overlapping periods of service. We used the term "short duration" and by that we mean either two or three years, although again we did not specify that.

Now, I think that those two matters to which I have alluded are the most important of all. We have made certain recommendations—I think five in all—for what we regarded as not general or drastic changes in the regulations as they presently exist, and we felt that no committee, constituted as we were, could properly undertake any general revision of the regulations even just relating to new drugs. We did make one recommendation with respect to bill C-3, dealing with the total proscription of L.S.D. and thalidomide in which we suggested that perhaps L.S.D. could be loosened up a little bit but with all the controls you want on it, and that thalidomide might be released to the experimental and laboratory field but not to the clinical field. As you all know, there is a mechanism whereby any drug that is proscribed may be obtained legally in this country, and all it requires is to get the assent of the cabinet. I gather that this could be a difficult feat on most occasions, but in fact there is such a mechanism. That is all, Mr. Chairman.

The CHAIRMAN: I am sure you would like me to say, on behalf of the committee, that we are indebted to these three men and to the Royal College of Physicians and Surgeons for the work they have done in the seven months they took to make up this report. I think we will throw the meeting open to questions generally and then we will try to speak specifically, starting with section 4 in the index, which is the concepts of new drug control, so that we can have some continuity. Can we have a general question on the chairman's statement?

Mr. BALDWIN: I wonder what you had in mind, Dr. Brien. Do you feel we could use the existing machinery provided by the amendment we made to the act last year to deal with the two drugs you have mentioned. Do you feel that the existing machinery, as we provided it by year's amendment or by this parliament's amendment, is now capable of effecting the purposes you have in mind?

Dr. BRIEN: I take it that you know that the only information I have is what I either heard on the news or read in the paper and that was to the effect that thalidomide would be released for animal usage and L.S.D. for either animal usage or for certain qualified investigators or clinics. Am I correct in that?

Mr. BALDWIN: Dr. Morrell might probably have the answer.

Dr. C. A. MORRELL (*Chief, Food and Drug Directorate, Department of National Health and Welfare*): So far regulations have been passed exempting L.S.D. from the total prohibition and providing restrictions on its distribution to institutions approved by the minister for use in those institutions by qualified

investigators under certain restrictions. Thalidomide has not yet been dealt with in any way.

Dr. BRIEN: So far as I am concerned, and I am speaking personally now, in so far as L.S.D. is concerned I would consider that this is adequate. As you might well suspect I have been bombarded by people who were interested in L.S.D. either from the standpoint of the treatment of acute alcoholism or, in some instances, the broader area of mental illness. I would be quite satisfied with its release under the conditions that Dr. Morrell has set forth. I would suggest, in reply to Dr. Rynard, that it can be a very useful tool in the investigation of either congenital defects on the one hand or perhaps in the inhibition of cancerous growths on the other, certainly in the laboratory field. Again, speaking personally at this time, I am not sure that I would go further than that, and there are very sound reasons for this which I am sure are known to all of you.

If we obtain good experimental evidence that it is useful in the animal field, then I think there might be occasions where it would be justifiable to release it under control. When one works in a hospital where they count the medicines three times a day, as they do in the one where I work, and in all hospitals in respect of controlled drugs, it is the wastage that bothers me. I am not concerned about somebody that wastes or gets away with a single pill. You cannot get away with a lot of pills. However, when you are dealing with thalidomide one pill is too many. This is one of the reasons why right now I would restrict it myself to the animal field unless you could convince the governor in council that a certain amount should be released to an individual to do a particular piece of work. If I were that individual, I am afraid I would keep it in my pocket and deal it out pill by pill. That is the only way I could account for my own conscience.

Mr. RYNARD: Dr. Brien has answered about four-fifths of my questions. Do I take it that there is the occasional one across Canada—and I think all of us have had letters from somebody—who feels that thalidomide is very useful in his case and that it has helped him more than anything else he has had? I had a letter from a lady, who incidentally was not a patient of mine, who had migraine. She now has her migraine back and cannot get thalidomide. I am wondering whether there is some way in which these persons could get this drug? I am wondering whether it might be the feeling of this committee that it could be done in such a way that it would not affect the dangers of it getting out of hand, but could be used, for instance, by such a person in a small dosage for a certain number of days.

Dr. BRIEN: This is very interesting. There is no doubt, in dealing with older persons, that thalidomide is an excellent hypnotic. I am sure that many of you have heard objections expressed in respect of its withdrawal. I do not know whether this is true, but I have been told that it has now been released for use in mental hospitals in Great Britain; whether this is so or not, I do not know. I am not worried about that, but I am worried about the persons working in the mental hospitals and the danger that some of this drug might leak out.

The thing that bothers me is the number of persons who are pill changers. I know four very prominent ladies who go to four different doctors and they exchange pills. This is the thing that makes you fearful in dealing with an individual such as your patient. If we could be sure that no one else but this patient would get it, then it would not worry me in the slightest.

Mr. HARLEY: Dr. Brien, you mentioned the setting up of an action committee of the advisory committee on drugs.

Dr. BRIEN: Yes.

Mr. HARLEY: And you mentioned that it became obvious to you that there should be some method of reviewing not only the new drugs coming on the market, but also the old ones. I am wondering whether, in your thinking, you would go a little further and say how you think this could be done at the present time.

Dr. BRIEN: Would you tell me what kind of practice you are in?

Mr. HARLEY: General practice.

Dr. BRIEN: One area which is very, very interested in this, as you can perhaps imagine from my remarks, is the Canadian pediatric society. They looked into this with great care. They actually submitted some most useful comments, particularly in the dosage field and other aspects which relate to children. The Canadian drug advisory committee, which I think has 14 members, meets relatively infrequently, one or more times a year. You cannot take this group. This is something which requires the kind of work that we have done and it needs somebody to sit down and go through all the things that worry the pediatricians in an effort to straighten them out. Sometimes these children need many more times the dosage proportionately than adults do and sometimes infinitely less. There are effects that nobody dreamed about at the time I was a student. There must be a long-term study with regard to whether a drug might have some effect in producing cancer, or leukemia, or perhaps affect pregnant ladies, and so on. The pediatricians are, of course, very interested in that too, because they get the products of the delivery to deal with.

I think there are grounds for looking at the whole drug structure, particularly as it relates to pediatrics. There are a whole lot of drugs that need to be looked at. For instance, there is the whole spectrum in respect of the effect on the womb, the kidney, and things like that.

Mr. MITCHELL: Dr. Brien, I am not one of these physicians, but I am a practising pharmacist. In respect of your suggestion concerning the standing drug committee, do you feel that the drug advisory board as now set up is not doing its duty? There are a number of these things and sometimes I feel there are too many committees. I happen to know that the drug advisory board is meeting today. Is that correct, Dr. Morrell? Do you feel they are not doing their duty? I do not feel—and I am probably thinking of the directorate when I say this—that another standing committee can add anything more than the drug advisory board that is sitting now.

Dr. BRIEN: I can tell you exactly what I think about this without the slightest hesitation. This is a committee which I believe is composed of 14 members—and you can look this up because it is set out by order in council. It has the power to appoint subcommittees; that is quite true. What we are asking is the appointment of a working committee—whether it be a subcommittee of that one or something else, I could not be in the least worried about that. It would need three, four or five, preferably an uneven number of members, who would get down and really slug at it. A committee that meets once, twice or even five times a year is not even going to scratch the surface of what we envisage needs to be and should be done. That is putting it in a nutshell. I am not for a minute being critical of the drug advisory committee. It has not been consulted nor has it acted in the fashion in which we envisage here. I think probably that would be a fair statement, Dr. Morrell.

Dr. MORRELL: Mr. Chairman, I do not think it was set up with anything like this in mind at all.

Dr. BRIEN: No. As a committee of the whole it is too big; I am sure of that. Also, if you were to go ahead and endeavour to get three, four or five people out of it, or two or three out of it and a couple from somewhere else, and

try to work at this, I think you would have a difficult chore. It was because we realized this that we made such an ambiguous motion.

Mr. MITCHELL: Could the answer to my question be that this advisory board might meet more frequently?

Dr. R. R. DUFRESNE, B.A.M.D., F.R.C.P. (Canada), (*Member, Royal College of Physicians and Surgeons of Canada*): No.

Dr. BRIEN: We have a member of it here, Dr. Dufresne.

The CHAIRMAN: Dr. Dufresne, would you like to elaborate on this?

Dr. DUFRESNE: I would like to repeat what Dr. Morrell said a minute ago. This advisory committee was not set up to carry out the type of task we are hoping to get from this standing working committee. As the task of this prospective committee is envisaged, we look upon it as a working group, as we have stressed and underlined the word, and this could not be accomplished by a committee which has the mere task of meeting once or twice a year.

Mr. MITCHELL: If this committee was flexible enough to handle the action you want the standing committee to handle, and met more often, would this be satisfactory?

Dr. BRIEN: What would you call flexible enough?

Mr. MITCHELL: So that it would cover exactly what you are asking for here, which you say they are not doing for the simple reason that they have not had the opportunity or that they do not meet often enough.

Dr. BRIEN: They have not been asked to do it.

Mr. MITCHELL: That is why I use the word "flexible".

Dr. BRIEN: In that case the word "flexible" would be enough.

In this country it is difficult to get people to meet often enough; this is a problem.

Mr. MITCHELL: I realize that, but I also realize that the setting up of too many committees does not always achieve what you want.

Dr. BRIEN: I beg your pardon?

Mr. MITCHELL: The setting up of more committees than you need does not always accomplish what one actually started out to do. I am not speaking of this particular committee, but rather many, many committees.

Dr. BRIEN: I agree.

Mr. MITCHELL: If they were asked, they could be given the flexibility to do it.

Dr. BRIEN: Yes, and they would also ask for the proper means to do it. These would have to be busy people—and I do not mean that the advisory committee is not composed of busy people, it is—and if you have busy people you have to get them together and find a way of fostering this kind of meeting. What we envisage would require, I would say, not weekly but semi-monthly meetings for a long time in order to get the job done.

Mr. RYNARD: I would like to ask Dr. Brien if the thought behind this—and this certainly has been my feeling—is that the material that would go before this committee would come from the universities, the medical schools and from research work—but primarily from medical schools—and pharmaceutical departments of the schools and universities across Canada. I am wondering whether that is true—and I surmise it is—and do you feel that the people who are dealing with drugs in the universities and hospitals across Canada, particularly at the university centres, should be the ones appointed? I wonder whether that might meet a number of the objections to this organization which Mr. Mitchell was mentioning?

Dr. Brien: There is a tremendous overlap of work in committees of this sort of which you are probably well aware. Here we have the professor of medicine from the university of Montreal on the drug advisory committee right now; there are other university people on it, of course; there are other persons from the university who are not medical persons or who at least are from departments other than clinical medicine, and persons who are completely outside the university. It is a good over-all committee. It is quite true that most of the information that is contained in that last appendix is from universities in the sense that it comes chiefly from faculties of medicine, faculties of pharmacy—there are 20 submissions from those two alone—and from veterinary medicine; some very cogent material has come from veterinary medicine. The dentists were less interested in it, although this is not exclusive at all; they are interested in mouth hygiene, of course.

Then the professional societies are greatly interested in this and they include men who are both in universities and out. One of the very important submissions came from the pharmacological society of Canada, which includes one of our members here; it also includes some of the spectators here this morning. It represents chiefly teaching, industry and investigation of one sort or another. So, this is not completely a university affair. The information we have collected has come from a wide variety of sources which we deliberately tapped. We tapped everything we could think of which we thought would be helpful. A committee to deal with these matters should not necessarily be purely a university committee or from a group of universities. It is very apt to have a fair number of people on it because they are the kind of folks whom you can lure into doing this sort of work. This committee here is a classic example of that. They are the only kind of people—I am not just making it exclusive of all the other areas—who have the time and the energy to devote to it. You cannot take someone who works by himself and put him at something that takes all the time we have spent on this for the simple reason that whatever he is supposed to be doing suffers, as indeed it has so far as we are concerned.

Mr. Rynard: Is there not a danger that this new committee might get into the same position of—I would not say chaos—lack of frequency of meeting that you have mentioned in respect of the other drug advisory board that is now meeting?

Dr. Brien: I am not sure. Dr. Morrell just said a few moments ago that it was not set up to do particularly the sort of job we figured this committee could do. It is quite true it has the power, as it is constituted, to set up subcommittees. We have just looked at the wording here. We deliberately tried to be diplomatic and, in fact, I discussed this both with Dr. Morrell and Mr. Monteith on several occasions before this was written because it is a very unusual recommendation to make.

We did not say that the committee was no good or anything of that sort, and that it should be replaced by another. We did not mean that either. The committee as it is now constituted and as it now operates is not doing this. If you could get out of it the people who would do what we want, then that would be fine. The thing we were anxious to do was to get this done, and if it could be done within the framework of the C.D.A.C., fine; and if it could take part of it, fine. But nobody on it would do it. I think the important thing is that if you set up this committee the people should agree to work on it and know exactly what they are getting into, and they are willing to do this. It is a real chore, let me tell you that. My wife is threatening to make an appointment to see me.

Mr. Nicholson: Mr. Chairman, I would like to discuss with Dr. Brien the angle pursued by Dr. Rynard earlier with regard to thalidomide itself.

Dr. BRIEN: Yes.

Mr. NICHOLSON: The doctor said very definitely, or I gathered the impression, that he thought that thalidomide was in the right place now, on the prohibited list, and is not even being released for use in laboratories. That leads me to ask this question: in the work of your committee, or in your medical research generally, have there been adverse side effects of thalidomide other than the one we associate with deformed babies, which leads you to that conclusion?

Dr. BRIEN: I can answer this again quite straight forwardly at least from such knowledge that I have. I said that I thought that thalidomide should be released to the laboratories, but not beyond because I am sure it is a useful tool, and has a place; and that if there was a suggestion that it might have a further useful place, we might subsequently take further action.

Now, the thing which led Dr. Kelsey to put a damper on thalidomide was not the problems that have rocked this country at all. It was, as far as I am aware, the fact that some paralytic phenomena were observed in people who had taken substantial doses over a period of three to six months, or something of that order. But they were adults; and this, I am sure has occurred. I cannot quote the figures, but I know it has been reported on multiple occasions, and only last week I got a letter from England, from friends of mine, on the outskirts of London. In this case the husband took what I am pretty sure was this. I am having difficulty with her writing. Not only doctors are poor writers; but I am pretty sure he has a multiple of these phenomena. By the same token, there is no doubt that it was very useful in my hands. In the time it was on the market, of course, I had no occasion to deal with the big labs; but in the older age group, it was a very useful agent, and we were fortunate that we had no side effects that I am aware of.

Mr. NICHOLSON: Is that a simple answer? Speaking as a layman, I am not a member of the medical profession.

Dr. BRIEN: I know.

Mr. NICHOLSON: Is that not an answer to the letters being directed to doctors and other members of the medical profession; that you are getting these other adverse and side effects? I know that in England there was quite a succession of newspaper articles about people losing the sense in the tips of their fingers and parts of their legs. So there would be danger even if a person was beyond the childbearing age, if he attempted to use it for migraine or anything else.

Dr. BRIEN: Yes, that is right.

Mr. HARLEY: I have two questions. First, to Dr. Morrell, I would like it if he could outline now what is the function of the drug advisory committee, and then Dr. Dufresne might tell us how you go about doing it, and if possible, give an example of a drug.

Dr. MORRELL: The drug advisory committee is now constituted or set up for the purpose of advising the food and drug directorate of the Department of National Health and Welfare with respect to any special problems which come up with respect to a particular drug or class of drugs. For example, should they be put on prescription, or should they not? Should certain action be taken with respect to drugs, and new regulations established with respect to a group of drugs? These were problems put forward to the committee from time to time when they met. No time consuming thorough study in depth of the food and drugs regulations or the act by the organization has ever been asked of the committee. We felt that sometime we needed advice,

as to what we should do in particular circumstances about a particular drug or class of drugs; and this is the type of thing that has been put before them.

For example, the drugs that are put on prescription—we have asked from time to time that the drug advisory committee give us a set of rules, for example, which we could follow in putting a drug on schedule F, which means that you can only get it from a doctor's order. And they have provided these rules, and I think this morning they are reconsidering them. We shall ask them also about drugs which are put on schedule G, or control drugs. We do not put a drug on schedule G until we have discussed it with them, unless there is a dire emergency, whereupon we would let them know what we have done as soon as possible. This is the type of thing done by the drug advisory committee in the past.

Mr. HARLEY: What is the position of that committee at the present time?

Dr. MORRELL: There are two members of the Canadian Pharmaceutical Manufacturers Association; two members of the Royal College of Physicians and Surgeons; two members of the Canadian Medical Association; two members of the Canadian Pharmaceutical Association; two members of a proprietary association, a manufacturer's association; and there is a member of the Pharmacological Society of Canada. The chairman is Dr. Cameron, while I am the deputy chairman, and there is a secretary from the department. Other members of the department sit in at the meetings, but they are not really members of the committee.

Mr. NICHOLSON: No members of the department of pharmacy of any of the universities?

Dr. MORRELL: The Canadian Pharmaceutical Association is represented by Dean Houston at the moment, and Jack Summers. Dean Houston is dean of pharmacy at the university of Saskatchewan, while Jack Summers is a hospital pharmacist. I think he was president of the society of hospital pharmacists a year or two ago anyway.

Dr. DUFRESNE: Would you mind repeating your question for my benefit?

Mr. HARLEY: Once the advisory committee has had a problem referred to it such as Dr. Morrell outlined, how does the committee then function? Is it strictly an advisory group, or would you go to a university and ask them to do research? Or do you go elsewhere for other things?

Dr. DUFRESNE: If you are speaking of my answer to this problem, problems have to be met, such as last year, for example, and it was, in some respects easy enough to say that a person could answer them without going to any university people about it, because I already have university people. But what I want to stress is that for any study in depth, a prolonged examination of the problem is necessary which would give the very kind of material we have covered, and I do not expect this advisory committee to reach for definite problems. Once or twice a year could do it as it is, and I hope you understand that. But I firmly believe that any members of this committee, who would be derived from it and set up as a working committee, could well do the job we are expected to do now. It is not because the members are not qualified; it is that the set-up is not leading to a proper—

Mr. HAIDASZ: Mr. Chairman, I would like to bring up another topic at this time. In reading through the report of the committee now before us I notice that the term "qualified investigators" is used.

I would like to ask, first all, whether the committee has had the opportunity and the time to investigate the problem of those who are investigating drugs in Canada at the present time; whether, in your opinion, they are qualified and whether you have found some of them unqualified, as well as whom in the future you would consider as qualified.

Dr. BRIEN: The American people, in tackling this problem, went at it diametrically opposite to the way we did. Are you familiar with Mr. Celbrezze's material? Mr. Celbrezze is the secretary of health education and welfare. He caused to be promulgated on August 10th last a series of proposals that related to the handling of new drugs, in which he set forth in great detail the methods by which they would be investigated and the qualifications of the people who would do it, and so on. He then set up a period of sixty days for people who were interested in this field to comment.

As you know, this committee went to see the F.D.A., which is the equivalent of our F.D.D., in Washington, on December 6th and 7th last. We were told they had had, I think, some 300 or 400 written comments and we figured, thousands of verbal comments, which were noted with respect to these regulations. Actually, they were changed on many, many occasions. In connection with the original form that they came out in I am perfectly sure, if I had been asked to investigate drugs under their terms, I would have said I would have nothing to do with it. And this is precisely what happened in the United States. A great many people who are very interested in drug testing, because the regulations were so minute and pernickety, said they would give it up rather than carry on.

And now, we deliberately have not defined "qualified investigator" here, and your question is a very reasonable one. We have interviewed people in a variety of societies or bodies who are intimately concerned with this and who are well known to us. When it comes down to the people who first investigate new drugs there is not a large volume. Although I cannot tell you the precise figures, the initial introduction of drugs into humans is rarely done in this country; it is done much more often, I think, in Europe and in the United States. So, there is a certain body of information available at the time that drugs are brought here. As we pointed out this is one of the reasons why people who are very capable of doing this are not as interested in it as perhaps they might be and perhaps they should be. As well, we gave other reasons which are there.

Now, in the initial phase, the critical phase of this work, the people who are most apt to do it in this country are those who are working in large hospitals, either in very specialized clinical investigation units, which are in a good many of our larger hospitals, generally teaching ones, or in the veterans affairs hospitals—and these basically are teaching hospitals as well, or in other specialized units such as in the case of my own hospital, the Victoria Hospital in London, Ontario. For example, I might cite the cardiovascular unit there. It is a most highly specialized one. That would be an ideal setting for the type of work you are referring to because the people who would be doing it have the necessary knowledge and the facilities. It is very important that they must have the facilities to enable them to prosecute the work with reasonable controls and they must have help to enable them to carry it out.

The Canadian Society for Clinical Investigation which is a national organization, embraces most of the young men and women as members, and they participate in the earlier phases of this sort of work in this country. I do not think it is fair to say that it includes them all; however, it includes the vast majority. These people are working in settings which, I would say in the main, are conducive to satisfactory work, or at least it could be so made.

I do not think that we should attempt to legislate down to the nth degree either the qualifications or the precise details of how it will be accomplished; I am saying this after having discussed it with a variety of people who, I think, are in a position to comment intelligently on it. I think that we have to put in some very wide power wherein we state that we recommend that the minister be empowered to either suspend a trial, or stop them altogether if multiple

ones were going on if he felt that this was wise. This might be on the basis of either unexpected reactions that occurred from the material being tested on the one hand, or it might be because conceivably somebody got into the testing field who was a bit out of his depth. I do not think you can legislate in this connection; you cannot legislate whether a person is capable or not of doing it. We have suggested, as in the past, the manufacturers be allowed to select their own investigators. This is the way it has gone on in the past. In the main, I am sure they selected good ones, and I am sure I have no reason to doubt that they will do anything different in the future.

We have suggested, with closer supervision, they must do something which they have not done in the past, namely filing not only the names of the people and where they are going to carry on the work but also what we describe as an outline of the objectives of the trial rather than the precise details, because I think if you make somebody file the precise details and then do not allow him to waiver a bit this will stifle research. Having talked this over with our Canadian Society for Clinical Investigation, as well as with Dr. Farquharson, who was initially the professor of therapeutics, then the professor of medicine at the University of Toronto, and now President of the Medical Research Council—and I might say I have known Dr. Farquharson for many, many years—it is our feeling that it is reasonable and proper to leave things as they are, with these suggested changes we have made.

I have been speaking here entirely as an individual in the last few minutes and I think it would be very worthwhile to hear what my colleagues have to say about what I have just said.

Mr. HAIDASZ: Mr. Chairman, to pursue this question of mine, Dr. Brien has stated that most of the drugs have had preclinical or clinical testing outside of Canada.

Dr. BRIEN: Yes.

Mr. HAIDASZ: And once they come into Canada there probably is much less work to do on the drugs.

Dr. BRIEN: Yes.

Mr. HAIDASZ: And thalidomide is an example of this. I am wondering whether clinical testing would have been prolonged a little longer if it had been done in Canada, and if it had been prolonged much longer than it had been in this country this tragedy probably would not have occurred in Canada. In other words, do you think that the drug directorate should test all imported drugs, what tests should be done, whether they should be done all over again—clinical and preclinical testing—and for a longer period than it is done now.

Dr. BRIEN: I might give you an answer to it in this way. This is the thirtieth year that I have practiced and I saw the first case of breast involvement from digitalis this year. However, this is no reason for taking digitalis off the market. It is an unexpected side effect that I have just waited thirty years to see. I do not think that another test on any drug is going to stop you from getting into the problem possibly that thalidomide caused. The only test subject which will tell you the answers you want are people. What happens in the case of chimpanzees—from the chimpanzee or the orang-outang down to the amoeba—is no indication that the same thing will occur in a human being, and you can go on testing ad infinitum.

I will admit that it would be very unreasonable to attempt to give humans something that kills everything else that you give it to in any dose whatsoever. However, the point is that you cannot test safety completely in respect of any drug. I do not think that any degree of animal testing would have prevented the thalidomide tragedy. The only way such testing would have prevented it

would have been to delay its introduction until someone else got it, and that is all.

You cannot tell whether an aspirin which your wife takes for a headache will not do this except that it has not been reported.

Interestingly enough I looked at an essay the other day written by a twelve year old girl with her left foot. She is one of five patients in respect of whom I have managed to gather data who have classical thalidomide deformities. In this instance I was able to talk to the young lady's mother at some length about the drugs she took while she was carrying this child. She turned out to have a classical phocomelia, or thalidomide deformity. The mother admitted having taken on occasions aspirin for her headaches and milk of magnesia for her bowels. Do you think we should remove the two of those articles from the market?

Mr. HAIDASZ: Mr. Chairman, at page 34 of the committee's report the last paragraph states:

> The committee feels that it would be highly desirable to require adequate clinical trials to be conducted in Canada before a new drug is released for sale in this country.

I wonder whether the chairman would care to explain what is meant by "adequate clinical trials"?

Dr. BRIEN: The reason we have included this paragraph is very simple.

As pointed out in the paragraph above, the directorate at times has had to release drugs, or has felt that it could not withold reasonable compliance when what would appear satisfactory trials had been carried out particularly in the United States, in respect of which a telephone conversation is easily carried on and, to a lesser extent, in the United Kingdom where it is much more costly and more difficult to do so, and actually where there was no opportunity to talk to the individuals who carried out the clinical trials.

I am sure that Dr. Morrell might have a certain degree of reluctance if he had any doubt about tackling someone in the United States, and in some way he would call in one of us, for instance, if we were engaged in animal trials. He might ask us by telephone or request us to come to Ottawa to discuss the whole problem. We think it would be a good thing from a number of points of view to have such confirmation, but at this stage it is obvious that you cannot make this mandatory even though it might be desirable. We think this would be good in the interests of the various provisions concerned in respect of the making, distribution and use of drugs to have the drugs adequately studied here and also from the standpoint of attempting to minimize but not eliminate, because I think you cannot eliminate, all possible ill effects. I think it would be desirable to have animal trials carried on whenever it is possible in this country.

At least one way to do this, to make it more attractive, would be to get the materials at any early stage when people are more interested in them.

I can assure you that I have never given a drug to a patient and been, as far as I am aware, the only one or one of two people to have done it, or something of that sort. I have never initiated the first animal trial on a human subject. I have done this on a few occasions when certainly there were not many other people using it in this country, but I had data from the United States or from the United Kingdom or somewhere else before I undertook such a step.

It would be to our advantage to have individuals at early or late stages carry out this testing in Canada so that the food and drugs directorate could make contact with them and discuss these things much easier.

The CHAIRMAN: Excuse me, Mr. Nicholson. You have been waiting for a long time, I realize. We are discussing item number 7 in the index with reference to clinical trials in Canada. I wonder whether it would be in order to limit our remarks to that subject, and then go on to a different subject? You proceed Mr. Nicholson.

Mr. NICHOLSON: I would like to ask the committee chairman whether in the course of their research they found anything in the earlier stages of the testing of thalidomide in Germany or in England which indicated that it had this affect of killing cells or of deforming the new cells that were being born?

Dr. SELLERS: I am not aware of any information of that type.

On the other hand, much of this information is submitted by the manufacturer to the appropriate government agencies of the countries concerned and is not necessarily published. As far as I know the first report about the cellular defects was published perhaps six months ago.

Mr. NICHOLSON: There was nothing during the first three or four years of work that would indicate that special tests should be made in the case of pregnant women, or preceding that, in the case of pregnant animals?

Dr. SELLERS: As far as I am aware there was no indication that this would be advisable. As a matter of fact, the acute toxicity of thalidomide, as you may have heard, is extremely low so that at that time it would naturally be looked at, as perhaps an ideal hypnotic. As we know, this was quite long.

Mr. NICHOLSON: Yet as it turned out after two or three years of general administration and wide scope use in Germany and or in England hundreds of abnormalities occurred?

Dr. SELLERS: I think this was after five years.

Mr. NICHOLSON: Yes, after five years. Thank you.

Mr. HARLEY: Dr. Brien, I am wondering whether you think there would be any advantage in including in Canadian legislation a clause making it mandatory that a certain percentage of investigational work be done in Canada, particularly in view of the fact that the drug directorate may not have sufficient knowledge of investigations being done in the United States and other places. I ask this question particularly in regard to the last two paragraphs appearing on page 35 of your report.

Dr. BRIEN: We were very careful at this stage of our report to make sure that we did not write in something that was not capable of implementation.

I am perfectly sure that if it is gone about in the right way more clinical trials can be carried out in Canada. I am sure of this fact.

We have made certain recommendations and have discussed this whole problem with a great many individuals who are interested in this regard. I would have no compunction at all in requiring that some work be done in Canada in respect of certain things. That is not specifically what we have said here. It is all very well for one to legislate that clinical trials will be done in respect of this, that or the other for such and such a reason, but I would not advise you to make legislation unless you can carry it out and that is the reason this is as it is. I do not think we should write something down that is not capable of implementation.

Mr. VALADE: Dr. Brien, you mentioned on page 33 it is quite clear that it is difficult, if not impossible, to have adequate clinical trials of all new drugs carried out in Canada at the present time. Well, this seems to be a little in contradiction of the desire as expressed up to now.

Dr. BRIEN: Yes, but you must realize that the people who are capable and are doing them might not be interested in doing them and there is no means of making them do it. If you ask me if I am interested in testing this drug or

that drug, I might say no to seven out of ten or to ten out of ten, and you will find that with everyone else in this country. This is the reason that is there.

Mr. VALADE: I did not want to make any inference on your good judgment. I was just asking this question because at a preceding committee meeting I asked the same question of Dr. Morrell. I asked him if it was possible to have a test of drugs carried out here in Canada and at the same time to have the same drug released in this country. This is what prompted me to ask this question: if it is possible, you are looking into the future but this is not available right now?

Dr. BRIEN: No, you see, from the standpoint of accuracy—and we will just confine ourselves to the new drugs—whether many drugs are released here with no trials at all or with very limited trials in this country, I am not in a position to answer that and I am sure Dr. Morrell can. But there are relatively few where the main clinical trials might be called perfectly adequate without reference to any that were done anywhere else. This implies that in a minimum of two different places which have no communication with each other, other than the fact that they will intercommunicate if they get into trouble right away, this is carried out very thoroughly. I am sure that the number is not great and I was not being belligerent at all when I said that I might not be interested in seven out of ten or even ten out of a particular group of ten. I think that for reasons we have given, that aspect of the practice of medicine, the actual use of medicine and how it operates, is much less interesting to a good many doctors than the mechanics of what makes you get into the trouble you are in. It is much less dramatic and so on, but I think it can be made more challenging and more interesting if we go about it the right way.

One thing that has bothered some people in clinical testing is the fact that they have dealt theoretically with a drug company. Obviously, if you are going to test the product, you must deal with it directly to get the materials to test. Sometimes they have been subsidized to varying degrees to help carry the work out. In the United States this has become a much bigger procedure of course than in this country, and some people have backed out because they began to wonder which was the cart and which the horse, the drug company or the university. We are interested in promoting more clinical trials. I think we do too few—I will state that right away. If we can set up some sort of a mechanism whereby there is a buffer committee, or whatever you want to call it, so that if we need aid—and we will for some things,—we can get it; then there is no doubt about it and the business can be carried out more or less on a basis where you can get grants for doing pieces of research. In this case the research would involve the use or the wisdom of using a drug. I think that it can be expanded but it is a thing that will grow slowly.

Mr. VALADE: During your study, Dr. Brien, have you found that in the United States there are some specialized organizations, purely outside of government control, that are conducting some clinical tests and are paid by pharmaceutical firms to do this research?

Dr. BRIEN: We did not specifically go into this, but I can tell you that there are. Dr. Sellers could probably answer this much more accurately than I. There are organizations, or in other words testing companies or corporations, that do this sort of work independently. I know that such facilities exist in the United States.

Dr. SELLERS: This is certainly true with regard to pre-clinical testing and chemical tests of a variety of sorts, but apart from university organizations or hospital organizations I am not familiar with any corporations that carry out clinical testing.

Mr. VALADE: I just have two more questions. I am sorry if I am taking up too much time of the committee.

Dr. Brien or Dr. Dufresne could possibly answer this question. Can a new drug be released on the market during an investigation? Is this happening? When a new drug is being investigated is it possible that this drug could be released for consumption on the market during the investigation?

Dr. SELLERS: I think the answer to this is that this is quite customary but not exactly in the way I believe you meant your question. The situation is this: if a pharmaceutical manufacturer acquires enough data, both clinical and pre-clinical, to submit a new drug submission to the appropriate authority and the authority agrees that the drug is acceptable for release, it is quite likely that clinical investigations, and perhaps pre-clinical investigations that have originated previously, will be carried on to their completion. So, in this situation you would have a drug released for sale and pre-existing clinical investigations carried on perhaps for several years after the drug is on the market.

Mr. VALADE: The purport of my question was to make the position that thalidomide was investigated and that these secondary effects were discovered after further and more acute investigations were made of the drug; but it certainly must have sustained some clinical testing before it went on the market without showing these effects which came out later on.

Dr. SELLERS: It is common practice in clinical investigation units to compare one drug with another even 50 years after either drug has been on the market in order to compare their relative effectiveness and, of course, the incidence of side effects or toxic effects. This, however, probably does not have anything to do with the interim use of a drug on the market as such. This goes on all the time. As I understand it, this is the type of study which suggested that thalidomide might have serious effects that had not been recognized earlier.

Mr. VALADE: My last question is this: Would your committee feel that there is a certain minimum of time required for clinical investigation of a drug? By this I mean is there a minimum amount of time in respect of safety for investigation of a drug before it is put on the market? I am talking about a potent drug now.

Dr. SELLERS: Mr. Chairman, my answer to this is that it probably depends a great deal on the particular drug and the intended use. If it is a drug that is to be given over a long period, the long term would necessitate, or suggest to me, that it be examined over a long period. Whereas, if it is a substance that is likely to be used once or twice for a very brief period for a specific purpose, perhaps for curing a specific infected organism, I should think in this case, if it was of great value, that one should be reasonably satisfied in testing such a material for a much shorter period of time. I think that your question has brought up a very important point; that it is almost impossible to lay out a precise pattern to which all drugs must conform in order to prove themselves to be of value therapeutically. The intended use and the duration of the intended use also are most important.

Mr. VALADE: Thank you.

Mr. NICHOLSON: Mr. Chairman, I would like to draw attention to page 47 of the report. Here they are dealing with regulation C.01.301:

> With respect to this section, the committee is of the opinion that the ultimate effectiveness and safety of a 'new' drug can be determined only by its use by a body of practitioners.

That is clinical testing. They are out of the laboratory and into the field of clinical testing.

Dr. BRIEN: On to usage. This goes on much beyond that, or it might. It might go on for years.

Mr. NICHOLSON: I continue:

> —over a sufficiently long period of time to enable qualified persons to make such an evaluation from accumulated data.

There you are talking about practitioners and they would be limited to doctors, dentists and veterinary surgeons.

Dr. BRIEN: Veterinary physicians.

Mr. NICHOLSON: You are away from the research chemist and manufacturing chemists. You have it in a clinical stage at that time.

Dr. BRIEN: Yes; it is on the market, it is out. This is the sort of thing; it is indeterminate.

Mr. MITCHELL: I would like to go back to number 6 and included with number 6 I would like to comment on number 10 which is in the second category.

The CHAIRMAN: Would you like to allow Dr. Harley and Dr. Rynard to ask questions first on clinical testing?

Mr. HARLEY: On page 36 under number 5 a point is brought up which we have touched on before. The last sentence says:

> —have been investigated adequately from the point of view of safety and effectiveness.

At the present time I understand the drug company does not have to prove a drug is effective. In other words, a drug has never been turned down in Canada because of some question as to its effectiveness. Would you comment on this?

Dr. BRIEN: Yes. I gather from speaking to Dr. Morrell that there might be times when he would withhold notice of compliance if the drug were completely inert; and he would do that on the basis, I think, that it was probably fragmentarily advertised and purported to do something it could not do. It is quite true the way our legislation is written—and this goes back to Dr. Morrell's original address which is an excellent exposition on the construction of that—that you got approval if you did certain things and did not do certain things; but it said nothing about whether it was effective or not. As a committee we feel that this should be added to it. It is not in our regulations and we think it would be highly desirable to ask that reasonable evidence be produced that the drug does what it is supposed to do, and that it is as safe as we can make it in the process.

Mr. RYNARD: Dr. Harley has covered the main part of my question. I was going to ask this: You feel it is still the main responsibility of the manufacturer to produce a clinically well tested drug?

Dr. BRIEN: Yes, sir; I do—we do.

Mr. MARCOUX: Dr. Brien, would you say, because most of the drug companies are world-wide companies and clinical investigations have been made in other countries, that would impair the interest of clinical workers here in doing some clinical research that has been done elsewhere? If so, would it be advisable that the clinical investigation in respect of drugs coming from other companies be conducted at the same time here in Canada, because we know those drugs will come on the market here in Canada, maybe after one or two years.

Dr. BRIEN: The answer to both questions is very simple; yes.

Mr. HAIDASZ: I have one last question on clinical testing. Has the committee in this report had an opportunity to find out whether pharmaceutical companies are studying the possibility of doing any tests for teratogenicity?

Dr. BRIEN: We did not make a specific study of that phase, but I think it would be very fair to say that we know that at least certain of them are interested in it. We know that two other groups are very interested in it, and they are the pediatric society, the Canadian society, the Canadian pediatric society on the one hand, and also the pharmacological society of Canada. They are very interested in that aspect of it; and the pharmacological society of Canada numbers among its members people who are in industry at the present time and people who are basically in universities.

I am sure that I cannot give you exactly what you want to know, but I am sure that they are interested in it; and I am perfectly satisfied that certain tests are being made, but I cannot give you an idea of the volume, and I cannot answer. Can you answer, Dr. Sellers?

Dr. SELLERS: From discussion with the medical directors and pharmacologists in the pharmaceutical industry I can certainly say that these people are highly interested, and that they are carrying out work actively in this field, but this is hearsay.

Mr. NICHOLSON: I have another question: is it not a fact, Dr. Brien, that most of these new drugs are put on the market by one or other of the large international drug manufacturing firms?

Dr. BRIEN: I think most of them are, but again I cannot give you precise figures.

Mr. NICHOLSON: If that is so, and if a manufacturer—a reputable manufacturer—has made complete tests either in the United States, Great Britain, Germany, or Switzerland, he is not going to repeat those same tests in other countries. We would never get those tests here, would we?

Dr. BRIEN: From conversations I have had with the pharmaceutical manufacturers themselves—we met them in their corporate capacity, their association—and in talking to them and to their medical directors on multiple occasions, and far out at the periphery, the people who come to see me, and the other doctors, are very interested to get clinical testing done in Canada.

Mr. NICHOLSON: Why would they? They are in the business of making money, and if they made a series of tests with which they were satisfied, let us say, in England, the United States, or somewhere, why would they repeat them in Canada?

Dr. BRIEN: I think the answer to that is that they might need it; on some grounds, it might be a bother, but on the other hand it is very sound business to be able to say that this drug has been tested in Canada—or any other country where you are trying to sell it.

Mr. NICHOLSON: Might it not be better for us to be putting more details in the hands of Dr. Morrell and to have them make their tests here? Is there any merit in that? Is it necessary that they duplicate or triplicate those tests?

Dr. BRIEN: Yes, yes; I think there are very sound reasons to have tests made in Canada. For one thing, the test in its entirety, or the testers may be seen by Dr. Morrell and interviewed on the one hand, and also there is no reason at all, why, if the facilities are here—and we have the facilities—why an international company would not be perfectly interested in having tests carried out in Canada or in the United States or Switzerland, or wherever else you like simultaneously, and I am sure that they would do this. But I do not think you should try to make this mandatory. I am sure that is right. You can

give Dr. Morrell the weapons, but you will end up having no drugs until you get the mechanics going.

Mr. NICHOLSON: I am not suggesting that the food and drug branch here would be testing, but they could refer it to McGill or the university of British Columbia, or somebody else to make these tests.

Dr. BRIEN: That is the point I am trying to put over. If we should set up adequate testing of the 180 odd products, or others and say that they will be included in the sense of the definition in that book, since there are alterations which make them new, if we were to test them thoroughly, and in the way that anybody would want them done in this country, I think you would set that up to have this carried out universally in one area or two, but not beyond three or four.

Mr. NICHOLSON: If complete tests have been made, let us say, in the United States, why should we duplicate those tests in Canada?

Dr. BRIEN: One reason—and I have the document here—is that it gives the final form of these rather onerous requirements which must be filled out by the testers, and one reason for this is that they have reason—and I would ask that this be dealt with kindly by the newspapers—sometimes to doubt the veracity of data submitted. I won't go beyond that.

Mr. NICHOLSON: That all goes back to the original point I made that it must be a reputable firm, and if the reputable firms have continued the practice over the years, it would not take long for an intelligent person to suspect something, and that sort of thing circles around very quickly; but if you know of a reputable firm which does this job well, let us say, in England or Germany, then there is no necessity for them to test it here. Would it not be better to have Dr. Morrell go to England or go to Germany to make sure that the tests have been done, and not have to duplicate those tests, with the vast expenditure of money. Is it necessary, in your opinion?

Dr. BRIEN: Are you speaking of this in terms of Dr. Morrell's building up a testing corporation?—I want to get this straight,—Or are you envisaging the testing being done in large hospital centres by a group of interested individuals or by the government, such as the national institute of health? What are you talking about?

Mr. NICHOLSON: I am talking about thalidomide. I presume it has been made in England, and it has been well tested in Germany and in England; and after a year or two of testing it is put on the market. This was done at the expense of the manufacturer. The manufacturer has satisfied the food and drug authorities in his own country and I presume he has satisfied our people here. Are you suggesting that we should duplicate that testing at the expense of the manufacturer again in Canada?

Dr. BRIEN: Not necessarily. What I am saying is that when he sets up testing, or when Dr. Morrell looks into this testing, or the food and drug authorities test in Washington, they are not taking a single test, they are taking two or more; that it might cost them considerably less to do some of that in this country rather than in the United States.

Mr. NICHOLSON: That is the other phase of it. I would like to see more of this work being done in Canada.

Dr. BRIEN: That is what we are trying to get at. However, I do not think we can do it by legislation right now because you cannot suddenly accomplish it all at once as we have not the facilities.

Mr. NICHOLSON: If the manufacturer which manufactures the drug eventually contemplates this drug being sold in Canada, why cannot he do some of that initial testing here rather than in Germany or somewhere else?

Dr. BRIEN: There is no reason in the world why we cannot if we can get the co-operation of the people to do it and also obtain people who are capable of doing it.

The CHAIRMAN: Paraphrasing one thing, you do not want duplication but clinical testing in the first instance done in Canada in conjunction with other countries.

Dr. BRIEN: It would be desirable if we could do some of it at the same time, as it is being done in three other places. I am sure that the F.D.D. here would be happier, in dealing with some of the tests, where they could make contact with the people who did them quite easily and where obviously they cannot if they are distant.

Mr. NICHOLSON: I had one further question along the same lines. Does the geographical and climatic condition factor have to be taken into consideration in connection with clinical testing? Might there be some drugs that would need special testing in Canada or in the northern atmosphere as distinct from the tropics or subtropics?

Dr. SELLERS: The activity of drugs is influenced by the environmental conditions or the extremes of environmental conditions and from that point of view it is easy to visualize, depending on the intended use of the substance, that this might be very desirable.

Mr. NICHOLSON: Is that not a broad category of division? We might be testing in that field rather than in another field, and if the drug is likely to be used in the tropics or subtropics, could there not be some division of this testing, and then let us test the drugs most likely to be used in this country. When you get into the tropics and subtropics you are dealing with forms of life like the amoeba, which does not bother you up here.

Dr. BRIEN: In principle, I follow your question and I agree with your line of reasoning. But I think it is impossible to spell out a pattern that will fit any instance that might arise.

I would like to add one comment to your previous question with respect to the necessity of testing drugs in Canada. I would not say it was a necessity but I do think there are good reasons for it being desirable, one being that our experience with the drug would accumulate in this country and our desire would not only be to make it acceptable to the F.D.D., but we would become experienced with its toxic properties, if any, and the side effects. If knowledge of this is readily available in this country to the F.D.D., or other persons using the drug in the field, it is a distinct advantage. And along your same line of reasoning, the doing of clinical testing of new drugs in conjunction with those done in other countries tends to make our pharmaceutical industry a more progressive one, and this is something which I think should be encouraged.

Mr. NICHOLSON: Thank you very much. You have given a very helpful and a very important answer to my question.

Mr. MITCHELL: As we are still on the clinical question, I would like to ask Dr. Morrell if it is not fairly common practice with the director at present to accept the records of clinical testing done in laboratories or other places by reputable firms manufacturing pharmaceutical supplies, as your specific necessary stamp of approval. Do you not take a number of their records as your symbol of having been correctly controlled and tested?

Dr. MORRELL: I am not sure that I really understand the question. However, our new drug submissions, which is the material that the manufacturer has collected of all the knowledge that is available about the new drug from all sides—and this, of course, is obtained in his laboratories or

in laboratories that he has employed to do the work, or by clinicians that he has managed to get interested in it—comes to us and we do accept their work. We think it is complete. You do not have to do each piece of work yourself; you get to the point eventually that you know what to look for. I think you can make a pretty good assessment as to whether the experiment or the trial or the information supplied is adequate or adequately obtained. But we, of course, do know from experience over the years what companies have the facilities and the capabilities of the personnel and what ones do use them to the best advantage. We can see it in their submissions. They probably give us on the whole much less difficulty than others.

I said the other day that I think that the majority—that is more than half—of these submissions that come to us we consider to be incomplete in some way, and so there is correspondence on them.

I do not know whether or not I have answered your question, Mr. Mitchell.

Mr. MITCHELL: I think you have. In other words, you do take in the introduction of new drugs by reputable manufacturing firms; you do take their records of their clinical testing to satisfy your directorate.

Dr. MORRELL: Yes, of course.

Mr. RYNARD: Mr. Brien, I wonder whether it is right to assume—and I think it is probable—that in the case of most of the drugs that come in from reputable manufacturers the obvious reactions have been noted and definitely those are the reactions that you are going to get within a few months or so. And I am wondering if by our clinical trials—and in the case of thalidomide it was three or four years before those things started to show up—we would be setting research back on some of those drugs, if we took the attitude that we have to try them long enough before we see these reactions. Now, I do not know what the score is on the immediate reactions of drugs, the mid reactions and the late reactions but I know myself—and I was in practice quite a few years—that it was a long time before I learned certain drugs were dangerous and that the odd person would react to them. I am wondering, if we took the hard and fast rule that we are going to test these things, whether we are not going to set research back, in which we are all so greatly interested.

Dr. BRIEN: Well, research with respect to the drugs will be prosecuted somewhere. It is our hope that more of it will be done in Canada. That is the first thing.

Your observation that it takes years to find out that many things are toxic, of course, is perfectly true and I feel it will continue to be true. Some of the more obvious reactions become apparent in acute and perhaps sub-acute toxicity settings. I think these things are found out by the animal tests. In respect of certain things that matter a great deal it is unfortunate that we are just finding out how chronic this can be. The people doing the testing in this regard are acting I am sure in the best of faith.

The CHAIRMAN: Gentlemen, I hope that we will be able to adjourn at 12:15 and come back after Orders of the Day so that we can conclude our questions of these three doctors this afternoon. They are very, very busy and have many other commitments.

Mr. VALADE: Dr. Brien, I should like to ask you just one short question in regard to that portion of your report which appears at page 36, paragraph 5. If I understand you correctly you are recommending that the manufacturers arrange to pay for clinical trials in respect of a new drug, and then you in part state:

> —it is in the public interest that trials be conducted, and be conducted in an adequate manner.

Is it your suggestion that the manufacturer set up its own clinical trial and research and that another organization parallel to this one would be established to complement those trials and research work?

Dr. BRIEN: No. What we envisage here, Mr. Valade, first of all is that the manufacturers do a great deal or most of the pre-clinical animal work as well as pharmacological or chemical work itself. When the research reaches the stage that it becomes reasonable to give a certain substance to humans, then the manufacturer may approach doctors who they feel will both be interested in and capable of carrying out trials to assist in the evaluation of the drug.

Mr. VALADE: Are you suggesting that a government body be established?

Dr. BRIEN: Oh, no.

Mr. VALADE: The last part of the same paragraph states in part:

> In exploring the best means of encouraging and supporting clinical trials, the medical research council should be requested to participate, and its president, Dr. R. F. Farquharson, has expressed a personal interest in so doing.

I should like to understand exactly what that recommendation covers, Dr. Brien.

Dr. BRIEN: Actually what that covers is the situation that our conversations from time to time with both the manufacturing association itself and the businessmen who run the companies as well as the medical directors who help them to run them indicate that some means should be worked out to encourage the carrying on of clinical trials in this country. It so happens that Dr. Farquharson is one of the very senior and nationally respected figures in this particular field. We were talking to him as an individual rather than as the president of the medical research council, and, although it might be interesting in certain aspects, it was felt that if we could get people interested in clinical trials and clinical investigations, it would be of advantage. It was felt by Dr. Farquharson and other doctors who represent the different firms that some plans could be formulated to make it easier to get these tests carried out.

Mr. VALADE: This to me seems to be invidious. Perhaps I do not understand exactly what the object of this memorandum here is. In what form will this body operate? Is it the recommendation that an independent privately organized group go into research?

Dr. BRIEN: No; that it set up a means by which it has been agreed or suggested to some extent at least, or to a large extent, that the manufacturers should pay for the testing of their products. In other words, get this done in a fashion that removes the direct connection between doctors and the manufacturer. We would interpose this body which had doctors and manufacturers on it and the doctors who work for manufacturers with some representatives of the medical research council to decide whether such a project was reasonable and whether it was worthy of support, and if so, to what extent, and look into the feasibility of determining how far this sort of program could be developed in this country.

Mr. VALADE: Thank you.

The CHAIRMAN: Gentlemen, it is now 13 minutes after 12 and we had decided to adjourn about 12.15. I wonder if it is in order to adjourn at this stage until 3.30 or whenever the Orders of the Day finish. I also wonder whether, when we do come back, we could stick to specific subjects as we have been doing so that we can expedite this.

Mr. VALADE: I propose we adjourn.

Mr. NICHOLSON: Mr. Chairman, at our last meeting I put forward the names of three possible witnesses who I suggested might be called in addition to the ones who have been called. One was Dr. George Ling. The others were Dr. Matthews and Dean Mervyn Huston of the university of New Brunswick. I am informed that Dean Huston is in Ottawa today and will be here for a day or two. I am wondering whether we should take advantage of his presence. It may be possible that he could stay over until tomorrow or Thursday and in that way we might take advantage of having him while he is here.

The CHAIRMAN: If that is the wish of the committee I would be happy to have the clerk or myself get in contact with this gentleman. It has been suggested that perhaps Dr. Morrell who knows where he is might speak to him in order to see if he could appear. I may point out that I believe from 3.30 this afternoon until 5.30 we will have a very full job in getting over this brief. I would not want to be presumptuous in telling this gentleman that he would be heard tomorrow.

Mr. NICHOLSON: I would prefer to have him on Thursday if he could be here.

The CHAIRMAN: Would you leave it with me to ascertain what we should do? We will adjourn until 3.30 p.m.

AFTERNOON SITTING

TUESDAY, February 5, 1963.

The CHAIRMAN: Gentlemen I see a quorum.

To expedite matters in order to get things off to a good start I think we should discuss sections 4 and 5 indicated in the index, concepts of new drug control and the present procedures of the department with respect to new drugs.

Dr. Sellers I think will deal with these two points as they are within his jurisdiction. I would ask him whether he wishes to say anything about these points in general, and then perhaps we could confine our remarks and questions to these points so that Dr. Sellers can keep other commitments he has made. Dr. Brien has stated that he will be happy to stay until his train leaves tonight for Toronto, if it meets our convenience.

Perhaps we could work out the details of our further meetings this afternoon in accordance with that suggestion. I hope that we will be able to complete our questions of Dr. Sellers so that he can leave as soon as possible.

Dr. SELLERS: Mr. Chairman, the only points that I wish to emphasize are two in number. Firstly, it is impossible to make any drug completely safe. There is a risk associated with the use of any drug or chemical. Therefore, the objective of any legislation is to minimize the risk, not to eliminate it, because this is impossible.

The second point I should like to make is that the introduction of new drugs I think is in the public interest, and our committee does feel it is in the public interest. Therefore, this is something that in general should be encouraged rather than unduly restricted.

To strike a nice balance between minimizing the risks yet restricting the introduction of new drugs to a minimum is a task that the government faces and, in general, I think that the procedures that have been followed are satisfactory in concept and have in general fulfilled the objectives that I have described.

That really is all I would like to say as to the points to be emphasized in respect of this section.

The CHAIRMAN: Gentlemen, perhaps we could confine our questions to those two sections, which I am sure you have read.

Mr. HARLEY: Dr. Sellers, on page 10, in the first paragraph, the last sentence states:

> Some sort of literature review and information retrieval section seem to be necessary.

Could you elaborate as to how you envisage that would work and tell us what the thoughts of the committee would be in that regard?

Dr. SELLERS: I think that is actually a quotation fom Dr. Morrell. Whether he would rather speak to his own suggestion or not I do not know. I can give you the practical details of what that means.

Mr. HARLEY: Did the committee particularly consider this aspect of the suggestion?

Dr. SELLERS: The committee considered the importance of a continuing follow-up on drugs, and the term used was "surveillance of drugs" not only during the time they are first undergoing clinical investigation but after notice of compliance has been issued and the drugs are on the market generally. By "surveillance" we mean the reporting of adverse reactions to the drug by physicians using the drug, to a central authority which we would assume would be within the food and drug directorate. We did not feel that it was possible to give a complete clearance to a drug and from that point on say that it is without risk.

Mr. HARLEY: Would you like to comment further in that regard, Dr. Morrell?

Dr. MORRELL: I certainly agree, Mr. Chairman, that we need to have some group of individuals charged with the surveillance of drugs on the market. At the present I think in our organization this is not the job or at least sole job of any particular person. We have been cutting our coat to suit our cloth, and to review literature, where these reports have been published, has been quite a task. I think that the United States food and drug administration has such a group in their bureau of medicine. Perhaps Dr. Brien knows how many individuals they employ.

Dr. BRIEN: I think they have three individuals in this regard at the moment.

Dr. MORRELL: Perhaps I could ask Dr. Brien whether they are literature scientists?

Dr. BRIEN: I cannot give you precise details, but I can say that they are physicians.

Dr. MORRELL: They have, somewhere in the food and drug administration, literature scientists reviewing medical literature, and I am told, and this is purely hearsay, that they review about 400 medical journals, or journals which contain articles that are certainly closely related to the medical sicences. This is quite a job.

When I made the statement that we need some sort of a literature review and information retrieval system I meant that we should have a group which is reviewing reports that come in, in journals and information that can be obtained from other sources. After this type of review the result should be brought to the attention of those individuals who are responsible for taking action.

We now have very little response directly from doctors in Canada reporting untoward reactions. We have sent out some letters to the doctors in Canada. I think the first letter was sent out by Dr. MacDougall a number of years ago when he was with our administration. We received very few replies.

I have sent out two letters in the last year. If letters were sent out to 17,000 individuals, we perhaps received 17 replies, or something of that order.

What I feel we need is some special group whose main function would be to review this information and keep us up to date as to what is being done. There have been many suggestions, which I do not need to go into now, regarding other ways of receiving information in respect of adverse reactions to drugs new and old.

The CHAIRMAN: I should like to direct a question for the purposes of clarification, Dr. Morrell. Do you envisage this as a department or group of people within your department, as an example, who would write all the doctors across the country asking for information regarding the side effects of thalidomide, rather than requiring the manufacturers to do this as has been the practice in the past?

Dr. MORRELL: It is a new policy, as far as I am aware, that the government should undertake to do this. I have felt that the law places that responsibility upon the manufacturers. I think that is a good principle, and still feel that manufacturers should have this responsibility, realize and accept it. However, things are changing and it may be that we will have to work more closely with the practicing physicians to obtain information directly.

The CHAIRMAN: Thank you.

Dr. SELLERS: Mr. Chairman, I think this is an area in which international cooperation might prove fruitful. I know that the food and drug administration is anxious to cooperate with the F.D.D. In this respect and I am lead to believe that authorities in the United Kingdom and other countries would like to see a greater exchange of information of this sort presumably through WHO.

The CHAIRMAN: A member of the world health organization I believe will appear before this committee toward the end of the month to discuss this problem.

Mr. NICHOLSON: I was wondering, Dr. Sellers, whether you have any suggestions to offer to the committee on getting favourable reactions to new drugs, not adverse reactions but some new side angle. I am thinking, for instance, of the drug dramamine. I mentioned it to Dr. Morrell the other day. As I understand it, dramamine—and I got it from one of the doctors who was in on the experimental work—was discovered on a train moving between Baltimore and Washington. They found that a person got rid of train sickness. They allocated it to the largest liner afloat with satisfactory results. This was 15 or 16 years ago. Have you any suggestions as to how we can follow up favourable reactions as well as adverse reactions?

Dr. SELLERS: Mr. Chairman, on the whole I would say this was covered reasonably well in the normal course of events, and that everyone, whether they be a manufacturer or a practitioner, is anxious to see that a drug that is administered is effective. If other favourable effects are observed by chance, I think it is most unlikely that this sort of information would remain buried. Indeed, there are many other examples of favourable effects that were not contemplated before the introduction of the drug.

Mr. NICHOLSON: Excuse me, Dr. Sellers, but Dr. Morrell did point out that of course the manufacturer would be interested if that were reported to him, and he also referred to the fact that you get great help from some particular

doctor who would pick it up and write it up in one of your professional magazines. However, are there not other ways of doing this?

Dr. SELLERS: In my opinion it is unlikely that any significant favourable effect would not be spread.

Mr. NICHOLSON: That it would not be drawn to the attention of your profession, I understand.

Mr. VALADE: Dr. Sellers, my worry is that before all these recommendations and considerations are implemented we may still go into a great deal of speculation and a lot of situations that we hope will never occur, but, as I said, there is no absolutism in drugs or in the safety of drugs, and I was wondering whether you had studied the possibility of working in cooperation with established medical and paramedical corporations with a view to elaborating this procedure that you are now envisaging. I am speaking now about informing for instance the colleges of pharmacists across the country or the medical profession throughout this country and trying to form a kind of national information centre with a view to working out some operative body that would implement these recommendations.

Dr. SELLERS: In the matter of obtaining more reports on adverse reactions, I think that the mechanism you suggest of making a definite effort through professional journals and through professional associations should be followed. As Dr. Morrell said, the response to direct mailed requests for reports on adverse reactions has been poor, but if it is possible to gain some reward from a tragic circumstance such as thalidomide, I think perhaps it might be said that the general public, as well as the interested professionals, are much more conscious now of an expected toxicity than they were eighteen months ago. I think this should be used to encourage more complete reporting. Is that what you had in mind?

Mr. VALADE: Yes. In respect of the recommendations you made I see that this committee is an idea which you studied with Dr. Brien and Dr. Dufresne. It is a plan that you are submitting for consideration for the future establishment of clinical controlled tests. It will be another body entirely different from what is actually existing. Is that right?

Dr. SELLERS: You are referring now to the standing committee or a working committee that we were discussing this morning?

Mr. VALADE: Yes.

Dr. SELLERS: I will be glad to add a few more comments about this subject. One of the real difficulties that the food and drug directorate has had is a lack of staff, and one of the real difficulties that they will have in implementing the recommendations that have been made is recruiting staff of a suitable type. This bears directly on the question which you asked me. In the recommendations we concurred with the request for staff made by Dr. Morrell, which, I believe, mentions 15 pharmacologists. Now, the entire output of professional pharmacologists in Canada at the moment—and I am using a doctorate as a criterion of professional status—is probably two or three per year. In other words, the recommendations that we have made suggest that the entire output of professional pharmacologists in this country will be recruited by the food and drug directorate. This is most unlikely because of such things as salaries, the competition from industry for the same individual and the competition from universities for the same individuals. In some respects universities and industry are more attractive to professional men of this type than is the food and drug directorate. I have used the pharmacologist as an example because the point I am making is the difficulty in recruiting enough individuals to implement the other minor recommendations, the recommendations which our committee has made to the Minister of National Health and Welfare. This

is a real problem and it points out the need to enlist the services of groups of individuals who may be employed by universities or elsewhere to be used at the moment as a source of quick advice for the food and drug directorate, at least until additional capable staff has been recruited. As I suggested, recruiting this number of professionally trained staff is no mean task. I regret to say that I do not think that the food and drug directorate will be able to recruit this number even within the time period of three years mentioned in the report. If they did, I think they would be doing extremely well.

The CHAIRMAN: In other words, you say there are three of these people per year who graduate and that we would be lucky if after three years we could get the number of people required. Who else would do the job other than having the food and drug directorate get these professional people or groups? Are there any other people below the doctorate level who would fill in the gap?

Dr. SELLERS: Well, this is an excellent and reasonable question. I think it would be most desirable to recruit persons with a doctorate, either Ph.D. or M.D., with special pharmacological training. This would mean you would expect to recruit from outside this country, and the source of supply is not nearly as good as it was a few years ago. There is the same demand in the United States; there is a similar demand in Europe. Therefore, it is unlikely that we are going to get very many individuals with this level of training. The only solution that is possible is to take persons with less training, or to institute training programs in order to train these employees who are on your staff. This is easier said than done. The making of recommendations that require services of individuals with specialized training is much easier actually than implementing the recommendations. I think it would not be unreasonable for this committee to give some consideration to the training of additional individuals in pharmacology and in perhaps clinical investigation so that these individuals would become available. At the moment as Dr. Brien said earlier there just are not enough individuals to go around.

Mr. ENNS: Would a program of fellowships tend to increase the output of the qualified person which is required?

Dr. SELLERS: To some extent: this would certainly help. The problem, however, is even greater than that. The amount of laboratory space that is available for this type of work at the universities and hospitals has become crowded because of additional students who are entering the existing schools; and the establishment of new medical schools with basic science departments along with them has not been as fast as it probably would have to be to meet the requirement for the basic medical scientist as well as the acknowledged requirement for the future.

The CHAIRMAN: Dr. Cameron indicated he might like to add something.

Dr. G. D. W. CAMERON (*Deputy Minister of National Health*): Mr. Chairman, in the department we have established a policy of sending members of the staff away for training. It occurs to me that the evidence now may be touching on a special situation where this technique would be of great value; that is to say that we would recruit to our staff people below the doctorate degree, young people with promise of advancement, and they could be given postgraduate training from the department. This is established practice and I merely mention it to remind members of the committee that this is a possibility.

Mr. NICHOLSON: Dr. Cameron has probably answered my problem. I take it, Dr. Sellers, that you do not have to be a graduate in medicine to do this work of which you speak; it is preferable but it is not necessary.

Dr. SELLERS: Yes. I think you have to separate the clinical and pharmacology which is carried out with patients and the laboratory investigations in

which an M.D. may be desirable but is certainly not necessary. So, both types of individuals are interchangeable to some extent.

Mr. NICHOLSON: If you had some person who has a good grounding and a special interest in science, even though he does not have the medical knowledge would he not fit into this slot under proper supervision?

Dr. SELLERS: Yes, sir. This is the usual course followed by someone who wants to take a doctorate of philosophy in pharmacology or in one of the other basic sciences. They enter from an honours science degree, biology or some other similar field, and spend three to five years obtaining a doctorate at which time one might expect competency to carry on independent work.

Mr. HAIDASZ: To follow the same line of thought, on page 32, the last paragraph reads:

> The committee further recommends to the minister that remuneration of the personnel be commensurate with the qualifications required...

Did the committee in its investigation meet with any complaints that the remuneration is insufficient for the job they are doing or should be doing, or that the remuneration is insufficient to attract these men with the qualifications we are looking for.

Dr. SELLERS: Mr. Chairman, the committee did not inquire into this aspect with specific individuals. I certainly am not the person to drect this question to for specific information. I do know the range of salaries that are paid by industry, by universities and the federal government for this type of position. The federal government's range of salaries is certainly not among the two highest.

Mr. HAIDASZ: In other words, in the opinion of the committee, perhaps in order to attract the personnel the salary ranges should be increased.

Dr. SELLERS: I think that this is almost necessary with the competitive situation which I have outlined in this particular field.

Mr. VALADE: Surely it is not only a question of salaries. It has been mentioned before that the industries are taking most of these people in their own services, and you have shown there is a lack of these people even in industries themselves. It is not a matter of salary. I think most of these people—I do not want to have people laugh—are educated men. Although we feel it might be a question of salary, it is only if we can get the men. The question is not salary at the moment, I think, but the men for the job. I think this is what should concern us more than the salary at the present time, if we cannot get the supply of talent we require.

Dr. SELLERS: This is quite right. Salary is certainly not everything. In addition to salary there is the question of conditions of service and the backing or the approbation of one's peers which is most important. It is something that I think the food and drug directorate deserves more of from its peers.

Mr. FAIRWEATHER: I have been interested in what to me as an observer seems to be sort of the national aspect or what might be a world-wide responsibility for research. Perhaps in 100 countries of the world committees such as this are not meeting, but might very well be meeting. Is there some aspect of this work that could take place in a sort of world health organization, say a clearing house of testing information and research?

It seems to me there is not anything very national about research. Are all the countries of the world trying to recruit these specialists? If so, might the solution be found through WHO?

Dr. SELLERS: Well, there are certainly many aspects of this which are of international significance and are not directly concerned in the introduction

of a new product. The first thing that is of national interest is: what are the reasons that congenital defects develop from the use of a certain drug; there are very many, many fundamental problems of toxicology which extend far beyond the introduction of one new drug or the interest of one country. I think an exchange of information in this field is desirable, and this is going on in WHO, as well as among the national authorities in most of the countries in western Europe and North America. The mechanisms are present. Again, I think it is the sort of thing that we should have in Canada.

Mr. FAIRWEATHER: In connection with the reading of scientific journals, surely there are not readers in every country of the world. Is there an area for a clearing house for what people have been saying in learned journals throughout the world. Is that now an area where you think something could be done?

Dr. SELLERS: This is almost a field of its own; it extends far beyond the drug field in the inter-communication of scientific ideas. The one aspect we are concerned with here specifically, I think, is covered with a sort of adverse reporting coordination centre which, by using an appropriate indexing system, could exchange specific information on toxicity of drugs internationally reasonably easily. If you extend this into the whole field of communication of scientific ideas I feel unable to give you the current state of this. There is voluminous literature on how to solve this very real problem.

Mr. MITCHELL: Mr. Chairman, I just wanted to comment on that. Could this question not be more appropriately put to someone from WHO, who will be a witness at this committee at a later date?

The CHAIRMAN: Yes, I suppose so. However, on page 18 there was some discussion about the WHO technical report and I think that is what Mr. Fairweather was referring to. I think Mr. Blanc of the WHO could probably give us a complete report of the whole aspect of this.

Mr. NICHOLSON: Not only in the report but more particularly in Dr. Brien's covering letter attention is drawn to the importance of using university staff and medical research groups at the universities. Is it not possible, Dr. Sellers, if it is going to take five or ten years to recruit the necessary staff recommended in your report, that a lot of this work could be referred to the different medical schools in Canada we are now supporting with taxpayers' money? Could not practically all these universities take on part of this load which Dr. Morrell and his staff are carrying.

Dr. SELLERS: This is a very reasonable question, Mr. Chairman, on a subject that I have thought a great deal about. I think if some specific contractual arrangements could be made it would be a good idea; but, for the reasons that I have mentioned before, namely the space problem and the increasing number of students, with the result of an increased student staff ratio—more students with the same number of staff—the universities have very real problems of their own. Now, I know my own department better than any other and our real limiting factor now is space. To some extent we have less recruiting problems. I think that our recruiting problem is relatively favourable, but we have no space or the space is limited. The same sort of comment can be extended to the other departments of pharmacology in this country. It will be some years before this changes.

Mr. NICHOLSON: Is it not a fact that in the field of medical research—and this is only one branch—most universities which are engaged in research work are reaching out for work. They are looking for new products and looking for grants from the research council to do work of this kind. I know that is the case of our own university out in British Columbia. Is there nowhere the two can be linked together to our mutual advantage in solving this problem?

Dr. SELLERS: In my position as head of a department of pharmacology, a particular department of pharmacology, I certainly am very interested in the question of financing a university department and, in going along a certain way, I feel that I would be bringing other matters to the attention of the committee. Now, I am not against this, I am quite happy to talk about financing universities.

Mr. NICHOLSON: All I am asking is this: if it is not an utopian problem, we should be doing something about it, and if it is an utopian problem let us forget it. But, is it practicable?

Dr. SELLERS: As I said, in relation to specific aspects being covered by contractual arrangement, I think it is possible.

Mr. NICHOLSON: Could not a committee such as you suggest in your report with the food and drug directorate try and work out a program of that kind?

Dr. SELLERS: This is one of the duties that I think they should undertake soon.

Dr. BRIEN: In respect of that particular point, Mr. Nicholson, that is one of the objectives that we felt might very usefully be pursued by this committee, however it came about. Perhaps initially we should just explore all the facilities available for testing at any level you like, not just in respect of patients, but also in respect of the facilities available to us in Canada, and the extent to which individuals presently operating them would be willing or interested in collaborating. I think until you get that sort of information you cannot come to any sort of sound conclusion, and we feel very strongly about that. There certainly is a need to make such an assessment.

Mr. VALADE: I should like to pursue this discussion a little further, Dr. Brien. I wonder whether it is possible to have a joint program in respect of the two sides of research or control? I have in mind the possibility of having universities take care of what they call *in vitro* experimentation, with the hospital research centres carrying on the *in vivo* experimentation. I realize that many hospitals have some type of research centre which would make such a plan possible.

Dr. DUFRESNE: What we are looking for now as far as hospitals are concerned is good clinical investigating units. If these do not exist we should like to see a group of men with proper facilities and clinical materials established to do the proper work. While I think it is only sound and safe to say that this does not exist in all hospitals, it does exist mainly in the teaching hospitals, so as a matter of fact this problem returns to the universities.

Mr. VALADE: Dr. Dufresne, perhaps you have not understood me. Is it possible that such a system could be established in respect of the hospitals and universities involved? I am sure that Dr. Sellers brought up the question of finance in good faith, and he said he would be very happy to discuss this question, but I am sure that most hospitals would be in a position to enter into this field. I realize, as Dr. Sellers has already stated, in order to get the right type of men this would involve a long range scheme over a period of perhaps five or ten years.

Dr. DUFRESNE: One must also find the men in the hospitals to do this type of work and they do not exist there today.

Dr. SELLERS: Mr. Chairman, normally a pharmaceutical manufacturer would deal with the clinical investigation in the hospitals and would be using the facilities of the hospitals. As far as using the facilities of universities for laboratory studies is concerned, the reason I said this was likely only in respect of very specific fields is that, in maintaining laboratories in the food

and drugs directorate, in the first place, it is only possible to check statements made in respect of new drug submissions, if it seems desirable to carry out research in appropriate fields, by using the talents of individuals who have become expert in these particular fields in order to review the new drug submissions or review the contentious questions in the drug field. If you farm all this work out to universities you would be detracting from a very important function of the central authority. Therefore, I do not think it would be desirable to farm too much of this work out. This is a central function that should be retained in the directorate.

The CHAIRMAN: Are there any other questions in regard to this specific point, gentlemen?

We will now move to the next section, that recommendation with respect to the expansion of the food and drug directorate. I think Mr. Mitchell indicated that he had some questions in this regard.

Mr. MITCHELL: Yes, Mr. Chairman, and I think perhaps the other two items I mentioned can be included in any comments that I wish to make or inquiries I put to Dr. Brien.

Dr. Brien, in your report you have stated that the expansion of the food and drug directorate is required, and you also take into consideration the suggestion of a division of the food and drug directorate. Do you feel that expansion is necessary and, secondly, that the directorate could be split into two sections perhaps because—and I think you would agree with me—an inspector of food would not need the qualifications that an inspector of drugs or new drug submissions would require?

Dr. BRIEN: To deal firstly with the need for expansion, I have not the slightest hesitation in stating categorically that I think it needs expansion in the worst way. They just do not have the man power to do that job which you and I expect them to do.

In respect of your second question regarding a division, you will notice that the committee did not make any very strong statement about that except to say that if it were contemplated it should be done only after a very careful look at all the factors involved.

If you read the appendices you will see that multiple recommendations have been made. One of those recommendations comes from an association of which I think you likely are a member, and is to the effect that the organization should be divided into food and drug directorates. We recognize the fact that there are half a dozen different submissions, or roughly that, which include such a suggestion. We did not sit down and devote any very prolonged or serious thought to the matter because in the first place we thought it was a bit beyond the terms of reference that were given to us, or at least we felt the main intent of the terms of reference did not include such a suggestion.

Secondly, we do not have the information which is relevant here, and certainly I think it would be fair to say that we would be very much opposed to any duplication in this field. I do realize that there are certain areas, particularly in respect of toxicology, for example, where one laboratory might be completely satisfactory having either two divisions or just one organization, as does exist today.

The feeling of the F.D.A. was that at the present time they would be against it. However, when you go to visit the F.D.A. you find that it is a giant compared to our own organization. If I remember rightly, it has 3,040 odd people, and these individuals are in various parts of the city—I am talking about their Washington arrangements—and they are certainly geographically divided right now. We just did not think this out to its logical conclusion, but I know that multiple bodies have suggested this.

Mr. MITCHELL: Dr. Brien, may I ask another question? Do you have definitely on record in the report to this committee that a separation of the directorate is necessary? Before you answer that, I would like to deal with an extract of the speech that Dr. Morrell has made. On page 7 he said "drugs are not dealt with entirely in the same way as foods". Now, to me, that indicates that there should be a definite division in this directorate. I realize the situation in which the director finds himself. I think that probably the budget has a great deal to do with it. At the same time I would like a recommendation that this at least be looked into if not implemented at some time because I have had a great deal to do with resolutions to the food and drug directorate, not recently but for some years now as an officer of the Canadian pharmaceutical association, and I think that they are sympathetic. However, your hands are tied as far as implementation of it is concerned. What I am driving at is that we could get some sort of definite recommendation which may strengthen your hand.

Dr. BRIEN: Where would you put the following situation. Take, for instance, a case where food has some residue in it that theoretically is a drug. Who would deal with that in divided set-up?

Mr. MITCHELL: If you are speaking of veterinary additives, I could tell you who could deal with that.

Dr. BRIEN: If you treat an animal with drugs and then there is some harmful effect, who would deal with it? I am thinking of dairy products here or indeed of the flesh of fowl or animal that has been treated with some kind of medicine. Where do you put that?

Mr. MITCHELL: I do not imagine these sections would be mad at each other. Could they not convene?

Dr. BRIEN: They are already amalgamated. For instance, I had a patient with chronic poisoning from apples that she ate which had been sprayed. She was a stout girl who was determined to become thin so she ate a great many apples and ate them all, including the core. I am sure she ate enough apples to get a pool of lead arsenic, or whatever the spray was. Ordinarily most of us would not have eaten enough to get the poison inside of us or else we would have thrown away the core and missed a good bit of it. Here again is an example. I am just producing some off-the-cuff arguments to show that it is not completely simple to separate food and drugs. I have no very strong feelings personally about the matter because I have not studied it that far.

Mr. MITCHELL: So that you would not want to say yes or no?

Dr. BRIEN: No, I would not.

Mr. MITCHELL: That is all I was asking.

Dr. BRIEN: I was trying to produce some arguments that show that it is not just a simple matter to split them from the standpoint of the work they do and also from the standpoint of economy. I sit on the fence and I admit it.

Mr. MITCHELL: I am only going by your recommendation here.

Dr. BRIEN: We went so far as to say that because multiple people brought it up the matter should be studied further.

Mr. MITCHELL: I would like to ask the same question of other witnesses and I presume that the committee would like to get the consensus. We have your answer now as being non-committal. That does not stop me from asking someone else.

Mr. FAIRWEATHER: He does tell us not to eat apple cores, which is a very great blow to me, I must say.

Mr. HARLEY: I was wondering about the words which appear on page 31 under No. 6. The third paragraph reads:

> The committee agrees that it is necessary to have the animal pharmacology and toxicology reviewed by specialists who are working actively in laboratories, and who should not devote more than one-third of their time to reviewing new drug submissions or in other advisory or administrative work.

Could you elaborate on that I was a little confused by it, I might say.

Dr. BRIEN: I think there are two points here in particular. I am sorry Dr. Sellers had to leave, but I think I can tell you what our feeling on that was. I am sure that the department does not now, nor probably will it ever, repeat a great majority of the study. It was our feeling that at times they might wish to repeat some of it right here, and in fact I think they do on occasion.

A point about the one-third-two-thirds business is very simply this, that from our point of view it is highly desirable to have people who are working actively in the field, in this instance of pharmacology, who are on the review board which passes whatever is up for study. The point is that if you do not keep those people working on it actively, I think they very quickly stagnate. This is a means for getting accurate and up to date work all the time.

Mr. HARLEY: You are implying here that the actual review by specialists or actively working laboratories would not be done by the food and drug directorate but by specialists outside of the directorate?

Dr. BRIEN: No, no, by some of the pharmacologists who are already there, and the additional ones that we hope in due course to get. They would advise Dr. Morrell of what they feel is the status of this product or that. But for them to give him the best possible advice, we think they should be working actively in the laboratories for the better part of the time, rather, so that they are progressing as scientists themselves rather than sitting behind a desk and looking at books.

Mr. HARLEY: Is there enough laboratory work to keep these people busy for the remaining two-thirds of their time?

Dr. MORRELL: There is no doubt about that at all; and in connection with this advice, it is these same people who we call pharmacologists that you are now thinking of as working entirely on drugs, yet they have a great deal to do with the toxicity of foods, and they will be working in areas which are overlapping and which are extremely important, because if later on the committee is going to talk about pesticides and residues, it will be the same group which will be testing the food; and moreover, where are you going to put vitamins? They occur naturally in food; but now they are prepared as pharmaceuticals as well. You have vitamins in food as well as in pharmaceuticals. This at present can be done by one division of the food and drug laboratories, but if you divide it, you will have one on this side, and another on that side who are doing the same thing.

The CHAIRMAN: If it were divided it really would not serve the purpose, and would only add to the expense. Is that correct?

Dr. MORRELL: I think you would have about twice the cost for, perhaps, not as good results.

Mr. HARLEY: I have one more question on this section. What do they mean by the expression "Pharmacologists—five man years equal 15 persons"?

Dr. MORRELL: If you have 15 men working in a food and drug laboratory and one-third of their time is spent on revision, you have the equivalent of five

men; but there will be 15 men, and dividing their time by one-third each, you have what I call five man years.

Dr. BRIEN: A lot of people had difficulty with that, and so did we.

Mr. VALADE: As director of the department of medicine of the university of Montreal, Dr. Dufresne, have you received many complaints as to the drugs which were used not meeting with the requirements of the food and drug directorate?

Dr. DUFRESNE: You mean from doctors?

Mr. VALADE: Yes.

Dr. DUFRESNE: Not in that capacity, no.

Mr. VALADE: Were there any instances when you felt that the college of physicians or yourself, as head of the medical department, should bring some of those discrepancies to the attention of the food and drug directorate?

Dr. DUFRESNE: I suppose this whole problem is one of communication, and we are talking about the same thing, as far as I am concerned. We have a working committee on drugs which meets every month. No new drug is allowed in the hospital without this committee seeing and approving it and doing any medical research that must be done on it. All this information goes back to the committee who transfer it to the manufacturer. So far no information of that kind has been sent to the doctors or to the food and drug directorate. It has all been sent to the manufacturer. They have been the ones responsible for bringing the food and drug directorate up to date.

Mr. VALADE: You mean that your committee on drugs has done the same inquiry or the same investigation through the facilities of the hospital itself to make sure of a certain degree of safety, or to check on the safety of a drug?

Dr. DUFRESNE: That is right.

Mr. VALADE: On page 36, section 5, there is an item which talks about the responsibility of the manufacturer. Later on it says that the manufacturer recognizes his responsibility. I have a hard time to reconcile that with the responsibility that the food and drug directorate should take, if there is a responsibility. In what way is it a responsibility? Is it in research, or in testing, or a legal responsibility for putting the new drug on the market? In the opinion of the committee where does that responsibility lie?

Dr. DUFRESNE: I think that in the opinion of the committee the first responsibility about a new drug—that is as to its safety, or its introduction—is in the hands of the manufacturer. Then the food and drug directorate, at the time of the submission of the new drug, has to look at the records, such as in clinical testing of the drug, and then deliver a note to the practice that the drug can go into the field at that time. I think that after a drug has been issued to the profession, the doctors themselves have responsibility, no less than we have, to notice all reactions, either good or bad, and of course report them. This has not been done officially yet.

Mr. VALADE: When you have doubt about a certain drug, about the safety of a new drug in your hospital, what do you do with that drug? Do you send it back to the manufacturer, or do you make a report?

Dr. DUFRESNE: So far I must admit that no report has been sent to the government. The manufacturer himself has always been advised first, and sometimes he is the only one advised.

Mr. HAIDASZ: On page 42, we read that "It has become abundantly clear to the members of this Committee as they have proceeded with this investigation that: (1): There is need for a careful and painstaking review of all drugs, not merely new drugs." Does that mean that there are some drugs on the market now which should be re-tested or reviewed?

Dr. BRIEN: The thing we are thinking about there above all else is in the main a review relative to dosage in children; a consideration in view of the development of cancer in some people where it has been wondered whether drugs played a role or not; the field of congenital malformation where the multiple effects of drugs would appear to be just one factor; and whether this was a very good time, first and foremost, to settle the problem with respect to drug dosage in children; secondly, to look at the drug over the whole spectrum, particularly paying attention to the ones which have been suspected by groups which have been suspicious, particularly from the standpoint of the relationship to cancer and malformation, and perhaps also to disturbances of the blood forming organs and so on. That is what we had in mind.

Mr. HAIDASZ: Did you run across any complaints about the side effects of penicillin lozenges? Has that ever been brought to your attention? In my practice I have seen reaction to them and I have read and heard that they actually do more harm than good, yet they have been allowed to remain on the market.

The CHAIRMAN: When you found side effects, was there any machinery under which the general directorate could govern the manufacture or quality, especially with respect to side effects? Was this done specifically in your case?

Mr. HAIDASZ: This matter was also brought to the attention of the annual convention of the Canadian medical association, and they have made statements about penicillin lozenges, yet the food and drug directorate apparently have allowed them to remain on the market.

Dr. BRIEN: Penicillin mouth was the name given to what we are talking about. In 1943, I made some home-made lozenges by taking agar and cutting it up and putting penicillin in it. It looked like fudge, and I gave it to the soldiers who had had acute streptococcal and other bacterial infections in their mouths during the war, and it proved to be remarkably beneficial and effective in a fair proportion of cases. It did not taste very appetizing I am sure, but it produced results. Occasionally we began to get some of the persisting effects that you are talking about. So this has been known, but interest in it has waxed and waned.

The last time I really took up the cudgels over this was with the minister of health of this province, not of this country. At that time I did not get very far. My main objection to it was not the side reactions you are talking about. The side effects came along, it is true; but it sensitized people so that when they had something that really mattered and you wanted to give them penicillin, it was not an impossibility but it increased the hazards of penicillin therapy a great deal. At one time I tried to get some local legislation passed, but did not get very far I am afraid.

Mr. HAIDASZ: Apparently penicillin lozenges now can be sold over the counter without a doctor's prescription.

Dr. BRIEN: Up to 3,000 units.

Mr. HARLEY: This is the worst kind.

Mr. VALADE: I am told that in the United States they are not allowed to sell over the counter ointments or lozenges that contain 1,000 units. Is that right?

Dr. BRIEN: I do not know. If you had 10 it would be just as bad.

Mr. VALADE: Perhaps Dr. Morrell would know.

Dr. MORRELL: They have on the market in the United States—because I bought them—some antibiotic lozenges. I do not know about penicillin lozenges, if you are speaking specifically of penicillin. I am not aware whether or not they have a prohibition against the sale of penicillin lozenges.

Mr. VALADE: The purpose of my question was to find out their standards in respect of ours and whether they have limited it to 1,000 units.

Dr. MORRELL: You say they do allow anything under 1,000 units?

Mr. VALADE: I think so.

Dr. BRIEN: From the standpoint of getting into trouble with reactions, I do not think it makes any difference whether a person takes one lozenge with 3,000 units or three lozenges with 1,000. There should not be any at all.

Mr. VALADE: My question was an attempt to find out on what basis we work in respect of putting a drug on prescription and on what basis they are required to put a drug on prescription in the United States. Do we have the same standards or are we more or less lenient?

Dr. MORRELL: The legislation in respect of prescriptions is not in step all the way along between the United States and Canada. There are differences on both sides. Sometimes we seem to be more strict and sometimes they do. The question of penicillin lozenges containing 3,000 units or less per lozenge was discussed ten or more years ago with what was the equivalent committee of the drug advisory committee. At that time I think it was the committee on pharmaceutical standards. The matter was brought to the attention of the committee and a study was made of the reports by members of the committee. There was literature and so on in respect of the sensitivity reactions which might have been produced by these lozenges; and when the data was submitted to the committee the matter just dropped. It was not thought that there was sufficient evidence to require the elimination of that from the prescription sale. It has never been brought before the committee since. I do not know whether it was ten or 12 years ago, but it was a long time ago anyway.

Mr. HARLEY: I think from what Dr. Brien has said various medical bodies at varying times have agreed that penicillin lozenges in this strength should be off the market. What representations could they make, or to what body would they make them, to have this considered by the food and drug directorate?

Dr. MORRELL: The drug advisory committee meeting today has two members from the Canadian medical association. One of the members is Dr. McNeil from the committee of pharmacology in the Canadian medical association.

I am sure the directorate would consider any recommendation from the Candian medical association to this effect.

Mr. MITCHELL: I think the pharmaceutical manufacturers have corrected that situation themselves. Speaking from a retail point of view I cannot remember when we have sold a penicillin throat lozenge for well over a year, but there are plenty of other antibiotic throat lozenges which have taken their place completely.

Dr. BRIEN: Yes. I think the tendency is to use agents that are used topically or locally, not necessarily all the time, but most of the time, and not ones that are very apt to be injected. The serious reactions to penicillin, the ones that are fatal or nearly so, not invariably but nearly always, follow the injection of a particular form of it. You can find a few fatal cases from penicillin taken by mouth, but they are pretty few and far between. The thing which triggers off the possibility is either the deliberate or inadvertent usage of penicillin at some prior time.

Mr. MITCHELL: In other words, you mean it tends to make them penicillin fast.

Dr. BRIEN: No. Here instead of making the germ penicillin fast it induces a state of hypersensitivity into that individual so that the next time they need it,

particularly in the injected form—procaine penicillin—the danger of a severe or even lethal reaction is tolerably high.

Mr. MITCHELL: You mean subcutaneously and not intravenously.

Dr. BRIEN: I just gave a patient 100 million units intravenously a day for the last week, but it is an unusual case. Usually it is subcutaneously or intramuscularly.

Dr. DUFRESNE: One more difficulty came from the fact that when taking those lozenges people very often did not know they were taking penicillin at all. If they did, then before injection when you asked them if they ever took it and had any reaction they would be able to tell you.

Mr. MITCHELL: If they did not know, then they did not read the label.

Dr. DUFRESNE: Why should they read it?

The CHAIRMAN: Gentlemen, I would like to have some advice about adjournment time. It look like we have a lot more to cover. Dr. Harley and some other members I believe have other questions. What are your views?

Mr. HARLEY: Personally I would be content to sit until six o'clock and see what we can accomplish.

Mr. MITCHELL: Mr. Chairman, I would prefer to sit until six o'clock in the hope that we would be able to finish.

The CHAIRMAN: Is that agreeable to the committee?

Mr. MITCHELL: I am afraid that there may not be many who would wish to be in attendance this evening.

The CHAIRMAN: Yes. If we sit until six o'clock I would hope that we could finish with these gentlemen because they have other commitments tomorrow.

Mr. HARLEY: We could go on until six o'clock and then reconsider the matter at that time when we know how much is left.

The CHAIRMAN: The only point I want to make is that there will be a vote at 8.15 p.m. and we will all want to be in the house at eight o'clock. Everyone has to eat. I do not want to crowd this all in by 6 o'clock and then have these gentlemen come back at 6.30 or any such thing as that, because I do want to get this cleaned up in so far as these two gentlemen today are concerned, if I can.

Mr. VALADE: In connection with this question of adjournment, Mr. Chairman, I wonder whether the committee members could point out what their main point of interest is, and then we could decide which one is more important. If we keep asking questions in the way we are we may not even end up at six o'clock with the completion of this report. It may be that some of the members would like to ask certain specific questions.

Mr. MITCHELL: I have only one question but it is not on the agenda, so I can wait until the agenda is cleared up.

Mr. HARLEY: I think we should go on to the recommendations, Mr. Chairman.

The CHAIRMAN: I was going to say the summary of recommendations commences at page 45 and I think it would be a good idea if we could bring this into focus.

Mr. HARLEY: Starting on page 47—I have no questions to ask in regard to the recommendation with respect to expansion of the food and drug directorate—

The CHAIRMAN: If I might interrupt, let us go through these recommendations starting at page 45.

The first recommendation is with respect to the expansion of the food and drug directorate. I think we have covered that very thoroughly with Dr. Sellers today.

The next recommendation is with respect to changes in the regulations at the present time. Do we have any questions on this recommendation?

Mr. HARLEY: Yes, I have.

Down the page, under (1), it says:

> Therefore, the committee recommends to the minister that after a notice of compliance has been issued, greater controls than at present be exercised with respect to the drug.

And you list them later. I notice there is some question about the time in here; you say: "such time as deemed necessary".

Dr. DUFRESNE: Yes.

Mr. HARLEY: What sort of timing do you anticipate?

Dr. BRIEN: This was something we discussed at great length with our friends in Washington and one of their recommendations was to the effect that when a drug was released it should be subject to review at three month intervals for a minimum of one year and thereafter at such intervals and for such time as the commissioner felt was necessary. And they made the point in this instance that there was no finite time at which it would necessarily cease with respect to any drug. It would be determined in the light of experience, and that was the reason it was written in the very indefinite way that it is. I do not think you can define it with precision ahead of tme.

Mr. HARLEY: What do you think would be the average then, approximately a year?

Dr. BRIEN: Yes. They have spelled out that it be reviewed at three month intervals for one year and then at subsequent intervals as determined by their experience up until that time.

Dr. MORRELL: This is a minimum of a year rather than a maximum.

Mr. HARLEY: Further down I notice that one of the controls is "dispensing by prescription only". This would mean that every new drug would be on a prescription only basis.

Dr. DUFRESNE: Yes, for one year.

Mr. HARLEY: Yes, but it would mean that every new drug, regardless of what it was to be used for, would be on a prescription basis for one year.

Dr. DUFRESNE: Well, that would be a reasonable period.

Mr. MITCHELL: Do you mean any drug?

Dr. BRIEN: Yes, anything that comes into the category of a new drug.

Dr. DUFRESNE: Of course, we would have to define what a new drug is.

Mr. MITCHELL: If you are speaking in connection with the tranquilizer field or the hypnotic field I would agree with you; however, there are many others classed as new drugs which, in my opinion, would not need a prescription.

Dr. DUFRESNE: How could you tell?

Dr. BRIEN: If you are thinking of marketing aspirin, which is a six and three-quarter grain tablet, it would be ridiculous to think of it in this way.

Dr. DUFRESNE: It says:

> Unless, in the opinion of the minister, such controls are unnecessary.

You can understand now why this paragraph was added. It is added to cover a situation where controls would not really be needed.

Mr. HARLEY: In connection with (2)(b), it says:

—indications that the drug is newly introduced, or a new formulation, on labels and promotional material—

Would you visualize a standard label on every new drug saying that if you have reverse reactions, notify your physician?

Dr. DUFRESNE: Yes.

Mr. HARLEY: This would be standard for any new drug?

Dr. BRIEN: Yes.

The CHAIRMAN: Is there some way a general practitioner could know what side effects there were without one of his patients saying he had an adverse effect because he used a new drug? Is there some machinery in control of this whereby he could inform the food and drug directorate of this side effect?

Dr. DUFRESNE: Yes.

The CHAIRMAN: Something could be worked out?

Dr. DUFRESNE: Yes, by local organizations and referrals.

Mr. VALADE: In the practice of a pharmacist there is always a difficulty. Of course, the prescription always binds the pharmacist himself. As you know, not long ago a doctor used a drug which was called liefcort which caused an awful lot of uproar and there was no way for an organization to control its usage by the doctors who used this product. Now this, of course, is a recurrence that could be expected and it does not seem to be covered by the present recommendations.

Dr. DUFRESNE: I think you know what happened to liefcort now.

Mr. VALADE: Yes. But, is there any provision for this kind of control. As you know, we are seeking safety and in this recommendation we do not seem to have it. I want to be quite fair to you; I am not casting any doubts on professional doctors. I am trying to find out if there is a provision or recommendation made to avoid this.

Dr. DUFRESNE: I am afraid there is nothing in this report.

The CHAIRMAN: There is nothing in this report to have the food and drug directorate control the practice of medicine in the province.

Dr. DUFRESNE: No.

Mr. VALADE: I am talking about the usage of a drug by a doctor.

Dr. DUFRESNE: You might talk about the manufacturing or the usage of it.

Mr. VALADE: I am saying the control on the pharmacists will be imposed by the recommendations through prescription. You control this drug in so far as the pharmacist is concerned but you do not control it in the doctor's office. The doctor is free to use this drug without any control whatsoever from the drug directorate or anywhere else.

Dr. DUFRESNE: You must differentiate between the fact that he is manufacturing the drug or getting the ingredients for its preparation ready and the fact he is using it or selling it.

Mr. VALADE: I am concerned with the fact he is using it and there is no control in that connection.

Dr. DUFRESNE: That is out of our terms of reference, I believe. This is the practice of medicine, not the manufacturing of new drugs.

Mr. VALADE: I am not clear in this regard. Perhaps I am just being stubborn.

The CHAIRMAN: I think Dr. Cameron and Mr. Curran covered this subject at the last meeting when it was suggested that it was not the responsibility of

the food and drug directorate to control the practising physician within the provinces, and that the terms of reference of this committee excluded that specific problem.

Dr. CAMERON: Mr. Chairman, there are two points involved in this regard. If a physician or anyone else manufacturers a drug for sale he comes squarely within the new drug provisions of the Food and Drug Act. If an individual compounds a drug in his own office to give to his own patient we would regard that as part of the practice of medicine, something over which we had no control at all.

The CHAIRMAN: The next recommendation is in respect of the establishment of a standing drug committee. I feel we have discussed this subject very thoroughly at the opening of Dr. Brien's remarks. Is there any additional question anyone has to ask in that regard?

Mr. Mitchell, would you just wait for one moment so that we have a quorum?

Mr. MITCHELL: I have part of the drug advisory committee waiting for me.

The CHAIRMAN: Perhaps before we conclude our discussions it would be appropriate for me to convey our thanks to the three gentlemen who have appeared before this committee today, and for the information that they have given to this committee. I am sorry if we have appeared to rush you gentlemen, and I assure you that it certainly was not the intention of the chairman to do so, but circumstances beyond our control required us to start a little later.

Mr. BALDWIN: Mr. Chairman, unusual diseases require difficult remedies.

The CHAIRMAN: I would like to thank Dr. Brien, Dr. Dufresne and Dr. Sellers for appearing before this committee. I am sure we will be able to digest their recommendations and incorporate them into our report when and if we make a report to parliament.

Dr. BRIEN: Mr. Chairman, I should like to suggest that when you gentlemen are looking at the list of appendices, the place where the meat lies is in item 48. The other items are very interesting but number 48, the very last one, contains a digest of the important material right across the board. There are 20 odd pages of the report under general headings but the main information is contained in the item I have indicated.

The CHAIRMAN: The appendices have been sent to all members by the Minister of National Health and Welfare in documented form for informational purposes.

Mr. MITCHELL: I thought it was a trucking company that was delivering that material.

The CHAIRMAN: Before we conclude our meeting may I have your wishes in regard to incorporating the report as part of this committee's hearings?

Mr. ENNS: Inasmuch as this material was sent out to the members of this committee in a separate form I think it would be very useful to have this report included.

Mr. MITCHELL: I would so move, Mr. Chairman.

Mr. HARLEY: I second that motion, Mr. Chairman.

Some Hon. MEMBERS: Agreed.

The CHAIRMAN: Do I need a motion to adjourn?

In order to make it quite clear I should state that we will meet at 9.30 in this room on Thursday morning of this week to further discuss the food and drug directorate unless I send notice to you regarding a change resulting from difficulties beyond the control of the chairman.

APPENDIX "A"

REPORT OF THE SPECIAL COMMITTEE ON NEW DRUGS

APPOINTED BY

THE ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF CANADA

AT THE REQUEST OF

THE MINISTER OF NATIONAL HEALTH AND WELFARE

DECEMBER, 1962.

The Royal College of Physicians and Surgeons of Canada

144 Iroquois Avenue
London, Ontario

January 18, 1962

The Hon. J. Waldo Monteith,
Minister of National Health and Welfare,
Parliament Buildings,
Ottawa, Canada.

Dear Mr. Minister:

It is with pleasure that I herewith enclose the report of the Special Committee on New Drugs, appointed by the Royal College of Physicians and Surgeons of Canada, at your request, last May.

This document and its appendices contain data and recommendations which are the result of many hours of work on the part of numerous bodies and individuals, whose cooperation was remarkable, and without which the work of the Committee would have been most difficult. In addition, all three members of the Committee were present on every occasion that it met. This report, therefore, represents a "team" effort, and the matter contained therein has been discussed, and revised, repeatedly, until now it has reached its final form after the most careful consideration.

The Committee has preferred to leave investigation and exploration of many important subjects to the recommended Standing Drug Committee and to the Food and Drug Directorate. These subjects include the exploration of means of encouraging and financing more clinical trials in Canada; the mechanism by which continued drug surveillance may best be carried out effectively; means of expediting the exchange of information on drug toxicity among countries; means of minimizing confusion in the nomenclature of drugs. All these matters are important but hinge on the most pressing problem—availability of qualified personnel to enforce recommended procedures and implement present recommendations. Obtaining suitable personnel will prove to be a major problem. Conceivably, some of these matters might be handled by contractual arrangement with educational, professional or research organizations.

The collaboration of the Medical, Dental and Veterinary practitioners must be sought in respect to reporting of toxic reactions associated with the use of drugs and potentially toxic materials, be they old or new. This is an ever present, continuing need. The solution is not legislative only, but is one of continuous education and continuous collaboration.

Our opinions have been based on the assumption that many of the basic decisions to do with control of new drugs are, in the final analysis, matters of judgment, not of definition.

We have attempted to limit as little as possible the legitimate distribution of a drug for testing purposes, but to make stringent limitations legally possible when this is necessary.

Our recommendations have been made after considering the number of investigators and institutions which might be considered "qualified" to conduct investigations in a country the size of Canada.

A safe, workable plan in this country might prove inadequate in a country many times larger. Attempting to legislate or regulate "in theory" regardless of practical considerations, makes administrative and practical difficulties accrue which are at odds with basic purposes. We believe that the introduction of new drugs in a proper way is in the public interest, and have based our considerations on this premise.

One might assume that in some cases the producer of a new drug might not agree with the decision of the Food and Drug Directorate. The Royal College Committee considers that a decision of the Directorate should be open to review by the Standing Drug Committee (if formed) and in the event of disagreement final decision should be with the Minister.

Yours sincerely,

(signed) F. S. Brien,
F. S. Brien, M.B., F.R.C.P. (C)
Chairman, Special Committee on New Drugs.

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Report of the Special Committee Appointed by the Royal College of Physicians and Surgeons of Canada at the Request of the Honourable J. Waldo Monteith, Minister of National Health and Welfare.

1. *Terms of Reference*

"To examine critically and objectively our present procedures for dealing with new drugs, the requirements of the Regulations, and any other matters that, in the opinion of the Committee, are relative to the issue. I should point out that the purpose of the new drug regulations is to ensure safety".

2. *Members of the Special Committee*

1. Dr. E. A. Sellers,
   Professor of Pharmacology,
   Head of the Department,
   University of Toronto.
2. Dr. Roger Dufresne,
   Director,
   Department of Medicine,
   University of Montreal.
3. Dr. F. S. Brien,
   Professor of Medicine, and
   Head of the Department,
   University of Western Ontario, and
   Chairman of the Special Committee.

3. *Procedure*

Initially, the Committee met with the Director and chief officials of the Food and Drug Directorate, to discuss in the proposed terms, the problems associated with the administration of the Food and Drugs Act, and the Regulations thereunder, particularly as they related to the problems of "New Drugs". The Committee then undertook to enter into correspondence with such bodies (at the national level, whenever possible), and individuals, as in its wisdom it felt could offer advice with respect to the problems contained within the above terms of reference.

These included:

1. The Canadian Pharmaceutical Manufacturers Association.
2. The medical Section of the Canadian Pharmaceutical Manufacturers Association.
3. L'Association des Fabricants du Québec de Produits Pharmaceutiques.
4. As many of the independent smaller firms as the Committee could locate.
5. The Canadian Pharmaceutical Association.
6. The Canadian Society of Hospital Pharmacists.
7. The College of Pharmacists of the Province of Quebec.
8. The Canadian Dental Association.
9. The Canadian Veterinary Medicine Association.
10. Connaught Medical Research Laboratories—University of Toronto.
11. L'Institut de Microbiologie et D'Hygiène de L'Université de Montréal.
12. The Canadian Medical Association.
13. The Canadian Society for Clinical Investigation.

14. The Medical Schools of Canada, through the Executive Secretary, Association of Canadian Medical Colleges.
15. The Deans of Pharmacy in all the Faculties of Pharmacy in Canada.
16. The Canadian Paediatric Society.
17. The Pharmacological Society of Canada.
18. The Canadian Medical Protective Association.
19. Mr. R. E. Curran, Q.C., Legal Adviser to the Department of National Health and Welfare.
20. The Food and Drug Administration of the Department of Health, Education and Welfare, Washington, D.C.

With the exception of the F.D.A. in Washington, these bodies, or persons, were invited to consider the problem presented to them, and to submit any comments that they wished to make, in writing.

In addition, several bodies, and individuals, having become aware of the existence of the Committee, and of its terms of reference, made voluntary, and unsolicited submissions to the Committee.

In most instances the bodies to which the Committee had written were asked to have several of their responsible officials, or representatives, meet with the members of the Committee to discuss the various aspects of the "New Drug Problem". Meetings were held, with all the Committee members present and the following bodies were interviewed:

1. The staff of the Food and Drug Directorate—on several occasions.
2. The Canadian Pharmaceutical Manufacturers Association, together with members from the Medical Section of this body.
3. The Canadian Pharmaceutical Association, which in part was represented by the President of the Canadian Society of Hospital Pharmacists.
4. The Canadian Society for Clinical Investigation.
5. The Canadian Medical Association.
6. The School of Hygiene, University of Toronto.
7. The Canadian Veterinary Medicine Association.
8. L'Institut de Microbiologie et D'Hygiène de L'Université de Montréal.
9. The Quebec Branch of the Canadian Society of Hospital Pharmacists.
10. The Canadian Paediatric Society.
    Société Canadienne de Pédiatrie.
11. L'Association des Fabricants de Québec de Produits Pharmaceutiques.
12. The Food and Drug Administration, Washington, D.C.

In addition the Chairman of the Committee inspected several pharmaceutical manufacturing plants, particularly from the standpoint of research, methods of production, quality control, etc. He also met with various officials in these plants and discussed the problem of drug safety. Considerable correspondence, and further submissions were received by the Committee from the bodies interviewed, and other interested parties.

All three Committee members, separately spoke with various persons from whom useful data could be obtained. These included members of the Medical Research Councils (Canada and United Kingdom), Ministry of Health (United Kingdom), and a representative of the World Health Organization.

The Director of the Food and Drug Directorate, Dr. C. A. Morrell, made available to each of the members of the Committee, copies of the Food and Drugs Act and the Regulations of the Food and Drugs Act (amended to

February 1962), and detailed copies of the present procedures used in the Department re New Drug Submissions (see Appendix 1).

4. *Concepts of New Drug Control*

The last item in Appendix No. 1 is a copy of an address by Dr. C. A. Morrell, entitled "Protecting the Consumer in the Field of Food and Drugs", delivered to the Consumers' Association of Canada Conference, Queen's University, Kingston—June 21, 1962, in which the functions of the Food and Drug Directorate are outlined. The following excerpts are worthy of inclusion in this report:

"the Food and Drugs Act is a consumer's Act intended to protect the consumer from health hazards and fraud or deception in the consumption or purchase and the use of foods, drugs, cosmetics and medical devices. It is not and never was intended to assist the producer, manufacturer or retailer in preparing or marketing their products". (1—paragraph 2—page 1).

"The Food and Drugs Act virtually does not permit the department to put a government stamp of approval on any food, drug, cosmetic or device nor to approve of any labelling, packaging or advertising. This is one of the reasons it is unlike some other federal legislation concerning foods". (2.—paragraph 3—page 1).

"The method employed by the Act and carried out in the Regulations is to make it an offence to do, or not to do, specific things. Since the law makes the omission or commission of specified acts a crime, the Food and Drugs Act is considered a part of Criminal Law and as Criminal Law it is within the authority of the federal government". (3.—paragraph 4—page 1).

"What I am saying, and I want to be perfectly clear about it, is that persons preparing or selling foods, drugs, cosmetics or medical devices are responsible for their products and for ensuring that they meet the requirements of the Food and Drugs Act and they will get no official approval if they do". (4.—paragraph 1—page 2).

"Another aspect of the law and its administartion needs to be made quite clear and to be emphasized, particularly at this time. Many people believe that because of the existence of the Food and Drugs Act and the Food and Drug Directorate that everything found on the market that is a food, drug, cosmetic or device has been approved and found to be quite satisfactory in every way. This is not correct. There is no guarantee in this field any more than there is a guarantee that no crime will be committed just because there is a Criminal Code". (5.—paragraph 3—page 2).

"Drugs are not dealt with entirely in the same way as foods. Indeed the section that deals with the safety of foods could not be applied to drugs. If it were forbidden to sell drugs having in or upon them any poisonous or harmful substances no active drugs could be sold. All drugs that have any effect at all are harmful to all people in excessive doses and they have the potential of being basically harmful to certain people in ordinary doses. Not only are there contraindications (conditions in which they should not be used) for most drugs but there are also dangers from known or unknown undesirable side effects. Is is well for the laymen, which includes the vast majority of people, to remember the slogan—"If it is not food it is poison". *Don't take* any drugs unless you have to". (6.—paragraph 5—page 4.)

"Up to the present, at least, it has been considered that all necessary precautions have been taken for the safety of the public if an acceptable new drug submission has been made and the drug meets the standard, if properly labelled and packaged and is required to be sold on prescription only* (which

* if Scheduled.

means it can legally be sold to a patient only on a doctor's order) and if doctors are made aware of the dangers of the drug." (8.—paragraph 6—page 5).

"Among the more important sections of the regulations, especially during the last few years, are those related to requirements for introducing new drugs. In these regulations new drugs are defined and the manufacturer is required to submit in a form, manner and content satisfactory to the Minister, all the information available about the new drug, including reports of his tests to show the safety of the drug when it is used in the way and for the purposes he recommends. This is called a "new drug submission". During the last eleven years, 1,883 new drug submissions have been received. There have also been many hundreds of supplements to new drug submissions". (9.—paragraph 1—page 6).

"These submissions are reviewed by members of our staff. If a new drug submission is found to be satisfactory the manufacturer is notified that the new drug submission complies with the requirements of the law and that he may sell the drug if he fulfills all other requirements of the Act and Regulations. Once again must I emphasize that a manufacturer is not told that his drug is safe. Many years of wide usage may pass before all the possibilities of the drug for good or bad are known. As further experience with the drug is gained, dangers not previously revealed or suspected may be discovered. In such circumstances the Food and Drugs Act requires *the manufacturer* to issue the necessary warnings either to the public or to the doctor". (10.—paragraph 3—page 6).

"Once a new drug submission has been accepted as complying with the law and no change is made in the drug or the claims made for it, there is at present, no legal support for demanding the withdrawal of that drug unless it fails in some way to comply with other requirements of the Food and Drugs Act and Regulations. On two occasions in the last eleven years the manufacturers have been asked by the Food and Drug Directorate to withdraw a drug. In both cases they have done so. In all other cases when drugs have been recalled, the manufacturer has done so on his own initiative". (11.—paragraph 3—page 6).

"Advertising". "It prohibits the advertising of any food, drug, device and even cosmetic, as a treatment, preventative or cure of any of a list of serious diseases. It is wisely held that anyone suffering from such diseases should consult his doctor for a proper diagnosis and treatment and that persons with something to sell should not encourage the public to diagnose and treat themselves for these grave conditions. Furthermore, delays in going to a doctor may have serious or even fatal results. I believe this section in Canada's law is unique". (12.—paragraph 1—page 7).

"When one considers the amount of work and the complexities involved, the administration and enforcement of the Food and Drugs Act can be frightening to contemplate." (13.—paragraph 2—page 7).

"At this point may I say that keeping informed of the significant advances in the world literature (medical and scientific) that influence our work is a monumental (yes, a colossal) task. How we are going to keep up with it is a problem we are now studying. Some sort of literature review and information retrieval section seems to be necessary". (14.—paragraph 3—page 8).

"Food and Drug is not a benevolent, all powerful, all pervasive protector that acts as a personal, immediate guardian in respect to every mouthful of food and drink you take or every pill you swallow. It is a "police" organization set up to "police" a great number and variety of products and industries for the purpose of bringing about compliance with the terms of the Food and Drugs Act, the Proprietary or Patent Medicine Act and the Narcotic Control Act. The essential purpose of our policing is to make the manufacturers and

dealers live up to these laws. No more and no less. *The manufacturer must accept full responsibility for his products".* (15. Paragraph 4—page 9).

Before forming an opinion on the suitability of these concepts and the present procedures for dealing with new drugs, it is appropriate to consider the interests of the various parties concerned.

First and foremost is the interest of the public, perhaps represented best by the patient who receives a new drug with the expectation he may receive benefit from it. His concern (although perhaps not expressed) is with his safety and with the benefit he expects to receive.

It is pertinent that from the moment of conception to the moment of death every individual is exposed to risks, sometimes involving life, which he cannot escape. Such risks obviously include, but extend far beyond, his exposure to chemical substances, whether such exposure occurs by accident or in the case of drugs, by design. It is not possible to eliminate risks to health or life but it is possible, and is considered in the public interest, to minimize certain of these risks, by various means. Clearly, an underlying purpose of the Food and Drugs Act is to minimize certain risks associated with the use of foods, cosmetics, and drugs. The concept of minimizing rather than the impossible objective of eliminating risks, is fundamental in any legislation of this type.

New drugs are produced with the object of improving the diagnosis, prevention, or treatment of disease and this objective is one which we consider to be in the interest of the public at large and one which the Committee considers should be encouraged rather than restricted by legislative procedures. It is unnecessary to expand this argument for the benefits which have accrued to mankind through the introduction of new drugs are common knowledge. Insulin, sulphonamides, penicillin, vitamin B_{12}, poliomyelitis vaccine, are but a few in a long list of substances which, by altering the natural history of disease, have altered the life history of man.

Nevertheless, the story of past successes does not alter the basic principle, that the public has a prime interest in the safety of new drugs, in their effectiveness, and in the way in which they are introduced.

The second group whose interests are involved, is the producer or manufacturer of new drugs. At the present time most new drugs are produced by large pharmaceutical manufacturers which operate internationally. This state of affairs is likely to continue. The costs relative to research and testing of a new drug are very high and competition among pharmaceutical manufacturers is keen. It is difficult for a small company to compete.

In Canada, most of the large pharmaceutical manufacturers are controlled from outside the country but, of recent years, several have made determined efforts to increase pharmacological and toxicological research, and to increase clinical testing of new drugs in Canada prior to general marketing. Both of these trends should be encouraged, rather than restricted, but with due regard to the interest of the public at large.

The pharmaceutical manufacturers differ from other commercial enterprises in that their products are concerned with the health and welfare of the individual directly, often at a time the individual requires immediate help. There is no doubt in the minds of the Committee that ordinary commercial aims, and the objective of supplying the best medicine for a sick person, become confused and require an arbiter. The relationship of effectiveness for the intended use, and safety in the way proposed for use obviously must be considered in each instance. Acceptable risks for any drug cannot be defined, for instance acceptable toxicity in an effective anti-leukemic drug would be completely unacceptable in an hypnotic drug. Thus the relationship of effectiveness to toxicity is truly relative and the acceptability of a drug becomes a matter of judgment, not definition.

The third group concerned directly with new drugs comprises the practitioners. The interest of the practitioner lies between that of the patient and the manufacturer. He is interested in the continued well-being and the improvement of his patient. If existing treatment is unsatisfactory, he must and should be interested in the introduction of new and improved treatment, yet he must prove that the new innovation is, in fact, better than the old. The ability to interpret experimental data, to safeguard the patient and produce evidence of clinical effectiveness, requires training, sympathy, and acumen beyond the ordinary.

5. *Present procedures of the Department with respect to new drugs.*

The present procedures of the Food and Drug Directorate with respect to new drugs are aimed at ensuring that the provisions of the Act, and Regulations under the Act (C.01.301; 01.302; 01.303; 01.304; 01.305; 01.306; 01.307) are followed. The procedures are described in detail in Appendix I and have been referred to in a general way in the previous section (quotation from a presentation of the Director).

For those who are unfamiliar with the process of introducing a new drug to the market it may be helpful to present an outline.

From a pharmacological standpoint, a drug may be considered to be an agent which modifies an existing biochemical or physiological process in the body, or in a microbiological organism present in the body. Thus, research on the fundamental nature of biological processes may suggest appropriate chemical substances which accelerate or inhibit a particular process. If the biological process is related to a disease, altering it may be expected to affect the disease. Often scores, even hundreds, or thousands of chemical compounds may be tested pharmacologically *in vitro* or in animals before one is found which gives indication that it might prove effective clinically. If a substance is found, its general pharmacological activity and its toxicity will be studied intensively prior to clinical trial. When these investigations confirm that the drug is effective, and the side effects (effects not related to the primary action) and toxicity warrant it, steps will be taken to arrange clinical trials.

At this point the manufacturer (for it is almost always the manufacturer who brings a drug to this stage) is required to inform the Minister (Food and Drug Directorate) of his intention to arrange clinical investigation. An identifying name or mark must be supplied to the Minister. The manufacturer is required to distribute the drug to qualified investigators only, who have facilities suitable for the investigation in question. He must keep records of the distribution of the drug and of the results of the investigation(s), and make these records available for inspection, to the Food and Drug Director on request.

Approval of the Director is not required, nor is the manufacturer required to supply more information than stated above. In spite of there being no legal requirement, usually manufacturers have filed with the Director an "Investigational Use Circular" which contains reasonably complete data on the nature of the drug, its toxicity, etc.

When sufficient evidence has been acquired

1. to ensure safety
2. to establish the dose
3. to define effectiveness
4. to define side effects and contra indications
5. to clarify the effects of overdosage

this information is compiled as the clinical section of a New Drug Submission. Together with data acquired from the pre-clinical studies, information on components, composition, methods of processing and packaging, facilities for control

(raw materials to finished product), stability, proposed labelling, and samples of the finished product, it comprises a New Drug Submission, which is submitted to the Directorate. Within 90 days the Minister (F.D.D.) is required to notify the person filing the submission whether the data and information comply with the appropriate provisions of the Food and Drug Act. If a Notice of Compliance is given, the manufacturer may sell the product, subject to other provisions of the Food and Drugs Act. With some frequency the Directorate has required further data. In some cases when a definite indication has existed the product has been listed in the schedules of the Act, restricting its sale to the prescription of a practitioner. Until very recently there has been no provision to suspend or withdraw a Notice of Compliance.

The responsibility of the Food and Drug Directorate is to review the submission as a whole and particularly to ensure that evidence has been obtained "to establish the safety of the drug for the purpose and under the conditions of use recommended." The "purity and quality" of the product, and the capability of the manufacturer to maintain these properties, and the claims made for the product, are also the subject of scrutiny.

The Food and Drug Directorate fulfils its duties by

1. Generally reviewing the submission.
2. Assigning specific sections to members of its staff expert in the appropriate branch of science applicable to that section, i.e., the clinical trials are reviewed by a physician; the pharmacological and toxicological sections by a pharmacologist; the analytical sections by a chemist.
3. A general review of opinions on specific sections, and the submission as a whole, by the Director with the advice of appropriate members of the staff.

The usual procedure is to request the manufacturer to supply additional information if some part of the submission is questioned. It is not customary for the data on pharmacological action, toxicity, or quality to be subjected to experimental confirmation in the laboratories of the Directorate. Usually there is no direct communication between the Directorate and clinical investigators.

Most new drugs introduced to the Canadian market have been developed elsewhere. This fact affects the problems presented to the Food and Drug Directorate considerably. Most if not all of the pre-clinical studies have been carried out in the country of origin, and most of the clinical trials have been carried out in other countries. Very frequently the product is imported into Canada in bulk, after manufacture in a foreign country. After importation it may be processed additionally in various ways, and finally formulated for market. Quite often finished products are imported and packaged in Canada. The significance of these facts is that intimate knowledge of the stages of production, of the individuals conducting testing or clinical trials is variable. It may be negligible, fragmentary or it may be virtually complete.

The following paragraphs illustrate the extent of information on production and control of drugs in foreign countries easily available to the Directorate (and to this Committee).

Excerpted from World Health Organization Technical Report Series No. 138

1. Egypt—Analysis by Government, but mostly on drugs entering Egypt only.
2. France—Control by Government. Regular drug plant inspections.
3. India—Federal control over drugs entering India. State control over domestic manufacture.
4. Japan—Analysis by Government.

5. Sweden—New Drug requirements.
6. United States—Federal control. Drug plant inspection. (see below)
7. United Kingdom—Government and industry control. Drug plant inspections for biological products. Export licences; probably no control exercised over exports. (see below).
8. West Germany—Loose Government control. Only poliomyelitis vaccine is strictly controlled.
9. Denmark—Government control very similar to that existing in Canada.
10. Italy—Theoretical strict control—in practice very little enforcement.
11. Holland—Government the largest manufacturer and carries out testing; has different requirements for exports.
12. Austria—Government control on some items.

These excerpts serve to indicate the variable controls on production of drugs, and the paucity of information on conditions actually existing in various countries.

The United States, the United Kingdom, Switzerland, and to a lesser extent France, West Germany and Italy are the major exporters of drugs to Canada. In some of these countries the control would appear to be good but the Directorate has no assurance that it is applied to exports. In the majority of foreign countries controls and tests on drugs intended for export appear to be the responsibility of the individual manufacturer. The same situation obtains for drugs made in Canada but intended solely for export to other countries.

Section 30 of the Food and Drugs Act states that the Act does not apply to drugs not manufactured for consumption in Canada and not sold for consumption in Canada, if the package is marked 'Export' and a certificate has been issued to the effect that the package and its contents do not contravene the laws of the country to which it is consigned.

Considerably more information is available of the situation existing in the United States and the United Kingdom.

United States—New Regulations respecting new drugs are being formulated but had not reached their final form when the Committee visited the Food and Drug Administration on the 6th and 7th of December, 1962.

See Appendix 2—"The Impact of New Drug Regulations on Physicians", by George P. Larrick, Commissioner of Food and Drugs, U. S. Department of Health, Education and Welfare, and Appendix 3—"New Development in Drug Regulation", by Ralph G. Smith, M.D., Acting Director, Bureau of Medicine, U. S. Department of Health, Education and Welfare, and Appendix 4—"Report of the Visit of the Royal College Committee to the Food and Drug Administration in Washington".

United Kingdom—Informal discussions were held by a member of the Committee with representatives of the Minister of Health and the Medical Research Council in September 1962. From these, and from other sources it appears that the controls of biological products are virtually the same as those in Canada and the U.S.A.; testing of vaccines, sera, etc. is carried out by the Medical Research Council. With respect to the remainder of pharmaceutical products the control would appear to be vested in the industry itself. The ethical practices of the industry and the Common Law are the safeguards on which the public depends. There is a considerable body of opinion that these safeguards are insufficient. Advisory Committees to the Ministry of Health exert considerable influence by advising practitioners of the effectiveness and toxicity of drugs. The free forum of the correspondence columns

of the medical journals have proven a valuable source of information of the side effects and toxicity of drugs used in practice. This has been peculiarly useful in the U.K., as compared with North America.

The procedures followed by the Directorate respecting imported drugs are outlined below.

Drugs in Schedule "C" (Insulin, Liver extract injectible preparations, Anterior pituitary extracts, Radio-active isotopes) and in Schedule "D" (Vaccines, Sera, Antibiotics for parenteral use) may *not* be imported into Canada unless the manufacturer has been licensed. A condition of the licence is that the manufacturing plant must be inspected by an officer of the Department. At the present time 46 foreign firms hold such licences (30 in the United States and 16 in Europe and Asia).

All such products are on a release basis (that is, each lot must be tested by the Department and found satisfactory before distribution), until sufficient evidence has accumulated that the drug meets the standard. In addition, an annual survey is made of all such products imported into Canada, with tests being carried out on representative samples. Up to the present time all of these products have been found to be satisfactory.

Drug plants manufacturing sensitivity disks (for use in determining the sensitivity or resistance of germs to an antibiotic) must be inspected and all lots are on a release basis. In addition, all antibiotics requiring certification in the United States must be accompanied by a certificate issued by the United States Food and Drug Administration.

Imported drugs not on Schedules "C" or "D" are controlled by 'spot checking'. Periodically, imported raw materials and finished drug products are sampled at Customs, and analysed. About 10% of drug importations are thus analysed. During drug plant inspections the Food and Drug Directorate examines the protocols on imported raw materials.

Short of testing every shipment of drugs that enters Canada the only manner in which the Food and Drug Directorate can have reasonable assurance that imported drugs are of good quality is to inspect every foreign manufacturing plant in the same way that it inspects Canadian drug manufacturing plants.

At the present time both foreign and domestic manufacturers of drugs listed in Schedules "C" and "D" of the Act must submit to inspection of their premises used for the production of these products before a licence is granted. The inspection is repeated annually, or even more frequently in the case of domestic and U.S. plants; yearly, or at least every second year, in the case of European manufacturers.

At present the detailed requirements for establishing the toxicity of a drug in animals for inclusion in a new drug submission are not covered in the Regulations. This does not mean there are not stringent requirements. The regulations (C.01.302.d; C.01.304.b) require detailed information of the 'test' establishing safety for the purpose and under the conditions recommended. The nature of the tests considered necessary, depends on the drug and its intended use, and the procedure presently followed by the Directorate is minuted (Appendix No. 1,, Pugsley, April 25th, 1962, attachment). The permutations of drug and intended use are limitless and in the opinion of the Committee make it inadvisable to alter the regulations by including specific standards of testing, or altering the actual procedures of the Directorate. The procedures of the Directorate will be altered from time to time with increasing knowledge of toxicological testing, by knowledge of the susceptibility of certain species of animals for certain types of testing, and by the development of tissue culture or other methods of testing toxicity. These procedures

or 'ground' rules of what is likely to be acceptable in specific situations should be available to manufacturers.

In order that knowledge of the validity of preclinical testing procedures may be increased, it is desirable that clinical toxicity should be correlated with the information obtained from using animals or from *in vitro* methods. This type of study is of obvious importance and should be encouraged within the Directorate. At present, because of an inadequate number of staff, the suggestion is impractical as a general procedure.

The procedures of the Directorate respecting new drugs are governed by the Food and Drugs Act, and Regulations, and in turn are influenced by the other responsibilities of the Directorate and the number and capability of the staff.

Mention has been made of features of the Act and Regulations which may warrant amendment or further study. Some recommendations appear later. In respect to other duties of members of the staff, the Food and Drugs Act is by no means limited to control of new drugs. The percentage of time and money spent on administration of the Act in respect to drugs, as opposed to foods, cosmetics and devices, is about 40% of the total. (See Section 6). The qualifications of the staff who review New Drug Submissions, are appended as Personnel Record Sheets (Appendix 43).

An additional duty, not previously mentioned, is the operation of a Poison Control Co-ordination Centre to co-ordinate information supplied to local Poison Control Centres in Hospitals across the country. The dissemination of information has been slow and this undoubtedly has affected the work of local centres adversely. The explanation lies in the discrepancy between responsibilities or potential responsibilities of the Directorate and the availability of qualified personnel to assume these responsibilities.

New Legislation or Proposed Modifications in Regulations in Relation to Procedures.

Recently an Act to amend the Food and Drugs Act (Bill C.3) has been introduced to the House. Its provisions make it possible to define the conditions under which samples of drugs may be supplied to physicians, dentists, veterinary surgeons or pharmacists. It is understood from the Director that these conditions will make it necessary for such persons to request a specific quantity of a specific drug. The Committee agrees with this legislation and the intent of the proposed regulation.

The Bill also adds a new Schedule ("H") of drugs proscribed for sale, and includes in the Schedule two drugs—Thalidomide and Lysergic Acid Diethylamide.

The Committee believes that the intent of this legislation is praiseworthy but could be achieved in other more appropriate ways. In its recommendations the same end, of limiting the use of a drug to certain qualified persons, is achieved without forbidding the sale of the drug absolutely. The Committee disagrees with absolute proscription of Lysergic Acid Diethylamide for investigational clinical use, and with the proscription of Lysergic Acid Diethylamide and Thalidomide for investigational use in animals.

The Committee has been informed that no other legislation or amendments to the Regulations with respect to new drugs is pending.

Proposed amendments to the Regulations regarding manufacturing Facilities and Controls have been circulated (Schedule 33) to manufacturers for comment. These amendments (C.01.051-.055) require that all drugs sold in dosage form shall have been produced and handled at all stages in suitable premises under strict conditions of quality control. Proper records and recall

facilities must exist. The Committee has not reviewed a final draft of the amendment but in principle agrees with the amendments.

Domestic and foreign drugs, new and old, would be affected, and inspection of plant facilities would be necessary to ensure enforcement.

In the Section on 'Concepts of New Drug Control', it was stated that it is impossible to eliminate all risks from the use of drugs new or old. It was implied that certain side-reactions are inherent in the action of drugs. The incidence and the seriousness of side-reactions, and the toxicity of a drug in relation to its effectiveness for a given condition are the factors which eventually decide the value of the drug. It may be many years before any unanimity of opinion exists on the value of a drug. Any decision as to value must be based on experience.

Thus with a new drug, it is desirable to continue some form of surveillance for a longer period than at present, when a Notice of Compliance with the laws of the country releases the drug for sale. A mechanism for continued surveillance should involve the Directorate, the manufacturer and the practitioners using the drug. A recommendation to this effect is made in this report.

Two questions may be asked.

Are the procedures as outlined, and as described by the Director to the Committee satisfactory to ensure that the provisions of the Act, and Regulations, respecting new drugs are enforced?

Are the provisions of the Act, and Regulations, satisfactory in translating into law the concepts respecting new drugs which have been expressed?

In the opinion of the Committee the procedures of the Department are sound, but, due to the lack of personnel and increasing volume of work, the present staff is inadequate to meet the demands placed upon it. Several members of the Directorate stated that this had led to a feeling of frustration. This will lead inevitably to a deterioration in morale and loss of efficiency, which, if not remedied, will compound the difficulties faced by the Directorate.

In general the Act, and Regulations, as interpreted currently, appear to have been efficacious and satisfactory. The concepts upon which these laws have been based, the concepts of the Committee and the concepts of the Director of the Food and Drug Directorate appear to be essentially similar. A fundamental difficulty is referable to the nature of the legislation itself. Insofar as property and civil rights are concerned the responsibility for drugs is a Provincial matter. The Food and Drugs Act is intended to protect the consumer from hazards to health, and from fraud and deception arising out of the sale of drugs. Certain things may be prohibited, but *authorization* or approval of others cannot be given. This imposes definite problems in controlling the manufacture of drugs, new or old. For instance, a drug has to be 'sold' (distributed) before it has to meet the requirements of the Act and Regulations, and this implies detecting the fact that it is sold. Registration or licensing of a manufacturer or product apparently (except for Schedules "C", "D", "G") cannot be covered by legislation of this nature. In the opinion of the Committee the Regulations of the Food and Drugs Act should be supplemented and extended as indicated in the Recommendations. Of necessity, the implementation of the Recommendations will demand corresponding alterations in actual Procedures.

The interests of the Provinces in the introduction and control of new drugs, and control of drugs generally, should be mentioned. In many ways this whole problem is recognized to be of international importance; a national control, let alone provincial controls, can be criticized on rational grounds. There is reason to believe that the Provinces recognize limitations in varying provisions of Pharmacy and other Acts and would be receptive to a co-operative approach to the control of drugs. The publication of standards for new and

established drugs, in nomenclature, assay, manufacturing control, deserves consideration and discussion by Federal and Provincial Authorities.

6. *Need for Expansion of the Staff of the Food and Drug Directorate and Recommendation.*

From a consideration of the data presented thus far in this report it is obvious that the responsibilities of the Food and Drug Directorate are almost overwhelming at the present time, in the drug field alone, and that the demands made upon it far exceed its resources.

Almost certainly, additional work, arising from the recommendations of this Committee with regard to new drugs and from other future recommendations relating to the control of drugs and chemicals, will be expected of the Directorate, and this will make the discrepancy between work load and man power even greater.

The details of the number of persons employed by the Food and Drug Directorate, and the percentage of time, and money, spent on drugs as opposed to foods, are given in Appendix No. 7, "Report to the Special Committee of the Royal College of Physicians and Surgeons of Canada on New Drugs", by Mr. A. B. Tennenhouse, Chief Administrative Officer, Food and Drug Directorate. In this report it is noted that some 410 persons (including 50 individuals in the Narcotic and Controlled Drug Division) spend approximately 42% of their time, and about 40% of the budget of the Directorate on drugs.

It would appear to the Committee that the most urgent need for increased staff, at the moment, is in the Ottawa Headquarters of the Directorate. In any expansion undertaken, however, the emphasis must be upon scientific excellence, rather than mere numbers, if the Directorate is to perform its functions more adequately. The recruitment of well-trained, suitable physician-pharmacologists, biochemists, pharmaceutical chemists (especially if these are medically trained) may prove to be extremely difficult. The availability of suitable personnel is likely to limit recruitment of staff more than the availability of staff positions.

The Committee has discussed the increased requirements of the Food and Drug Directorate, repeatedly with Dr. Morrell, and other senior members of his staff. In making its recommendation it has considered, most carefully, the additional help needed to review new drug submissions, and the hazards arising from the use of drugs.

The Committee agrees that it is necessary to have the animal pharmacology and toxicology reviewed by specialists who are working actively in laboratories, and who should not devote more than one third of their time to reviewing new drug submissions or in other advisory or administrative work.

The Committee further believes that collaborative studies (with respect to both animal and human toxicity) could be devised, and carried out by individuals working in the Directorate, University centres (in both the basic science and clinical fields), and the pharmaceutical industry.

RECOMMENDATION:

The Committee recommends to the Minister that immediate steps be taken to increase the personnel of the Food and Drug Directorate by the addition of properly qualified persons. The Director has stated the following requirements and the Committee concurs with the recommendation.

I.—*Medical Section.*

(*a*) Two physicians.
(*b*) Two veterinary physicians.
(*c*) One chemist.
(*d*) One technician.

(*e*) One stenographer.
(*f*) Four clerk-typists.

II.—*Laboratory Divisions.*

(*a*) Pharmacologists—5 man years=15 persons.
(*b*) Pharmacists —3 man years= 9 persons.
(c) Bacteriologists —1 man year = 3 persons.

The Committee realizes that it may be difficult to recruit the above personnel in under three years.

The Committee further recommends to the Minister that remuneration of the personnel be commensurate with the qualifications required, and that such additional facilities be provided as, in the opinion of the Director, are necessary for the proper functioning of these additional personnel.

7. *Clinical Trials in Canada.*

In the interests of public safety the Committee believes that it is desirable for at least some of the investigators conducting clinical trials to be readily available for consultation, if necessary. Access to investigators in other countries might well present difficulties. In addition, fostering the development of a comprehensive pharmaceutical manufacturing industry in Canada is in the national interest.

With respect to "new" drugs the Directorate desires but does not require reports of clinical trials conducted in this country. However, this has not been feasible in every instance. From conversations with representatives of the Canadian Pharmaceutical Manufacturers Association, L'Association des Fabricants du Quebec de Produits Pharmaceutiques, the Food and Drug Directorate, and other bodies and individuals, it is quite clear that it is difficult, if not impossible, to have adequate clinical trials of all new drugs carried out in Canada, at the present time.

The reasons for this difficulty are multiple, and include:

(1) Philosophic considerations with respect to drug testing; it is commonly believed that testing is less challenging, less interesting, and of less scientific value than investigation of the nature and cause of disease. This view is held particularly by those best suited to carry out clinical trials, i.e., by the staff of University, teaching, or other large hospitals.
(2) The lack of adequate personnel or the requisite facilities to carry out the detailed studies and controls necessary to the proper conduct of clinical trials.
(3) The lack of financial support for such trials or the reluctance to accept such support directly from a pharmaceutical manufacturer.
(4) The fact that many "new" drugs have been tested extensively, in other countries, before their introduction into Canada. This makes detailed clinical trials less attractive to Canadian investigators.

In view of this situation the Directorate has had to make certain of its decisions with respect to the release of new drugs on the basis of clinical trials conducted in the United States, to a lesser extent in the United Kingdom, and with but scant information from Canadian sources, or even none at all.

The Committee feels that it would be highly desirable to require adequate clinical trials to be conducted in Canada before a new drug is released for sale in this country. It also realizes that it is not feasible to make such a recommendation mandatory at the present time. It does, however, recommend that some means be established whereby the clinical testing of new drugs in Canada can be encouraged on an increasing scale, to achieve this end.

The Committee has considered methods by which the clinical testing of drugs could be encouraged in Canada, and has discussed this matter with various bodies and individuals and would make the following comments:

1. Already, there is a considerable amount of Clinical Investigation being carried out in this country. There is a need for much more work in the general field of the investigation of disease processes and this investigative work should be extended to studies of their specific therapy.
2. Some clinical testing of new drugs is being done by the members of Clinical Investigation, or similar highly organized, Units of the larger hospitals, at the present time.
3. Additional clinical trials are being conducted in other settings, ranging from studies on patients admitted to teaching hospital beds, (but not in the highly specialized units mentioned in paragraph 2), or in the out patient clinics of hospitals, and, in certain instances, in patients being treated by physicians in the course of their private practices (and this could be, therefore, in the doctors' offices, the patients' homes, or in hospitals, or any combination of these settings).
4. There is an urgent need for collaboration on the part of all bodies concerned with, or interested in, the clinical testing of the new drugs (which, in its simplest form, means those concerned with the production, distribution, control, investigation, and use of these therapeutic agents) to assess the magnitude of the problem, the facilities presently available, the expansion necessary to enable adequate clinical trials to be carried out in Canada (in terms of personnel and additional facilities), and the roles which each could, or would, be willing to assume in this matter.
5. It is the responsibility of the manufacturer not only to ensure that the quality of the pharmaceutical products produced is controlled properly, but to ensure that these agents (whether they be in the "new" drug category or not) have been investigated adequately from the point of view of safety and effectiveness.

   The manufacturers recognize their responsibility and state that they are willing to assist in the expansion of facilities necessary for the proper conduct of clinical trials in Canada. While it is the responsibility of the manufacturer to arrange and pay for clinical trials of a new drug, it is in the public interest that trials be conducted, and be conducted in an adequate manner. In some instances it can be visualized that the public may have an over-riding interest in the results of such a trial. In such a case the expenditure of public funds, and the collaboration of an agency of the government in conducting the trials, would seem reasonable. This, in the opinion of the Committee, would be rare, and should be restricted to drugs which give promise of preventing, alleviating, or curing some disease in a remarkable way. Penicillin, cortisone, poliomyelitis vaccine, might be cited as examples. If the occasion arises, the Medical Research Council might be an appropriate agency to co-ordinate such trials.

   In exploring the best means of encouraging and supporting clinical trials, the Medical Research Council should be requested to participate, and its President, Dr. R. F. Farquharson, has expressed a personal interest in so doing.
6. It is the responsibility of the Food and Drug Directorate to evaluate the results of the preclinical and clinical tests, and to require the submission of further data if, in its opinion, those made available to it do not warrant the issuance of a Notice of Compliance.

The present views of the Directorate with respect to its responsibilities for New Drugs have been discussed, on repeated occasions, with the Committee, and the latter concurs with the view that these should remain the same as in the past, "Namely to review and evaluate the data and information provided by the manufacturer to establish the safety of use of the drug for which it is proposed or recommended". See Appendix No. 6—(a) "Responsibilities for New Drugs". This document also contains the details of how the Directorate contemplates that this aim can be achieved. The Committee believes that 'outlining the objectives' of a proposed clinical trial is preferable to an 'outline', paragraph 4(*b*), on page 1, Appendix No. 6(*a*).

The Committee further believes that, in exceptional cases, the Directorate should have the power to limit clinical trials to certain qualified investigators and to suspend a clinical trial when it is in progress. It should also have the power to suspend or withdraw a Notice of Compliance, in which case the drug should revert to investigational status.

8. *The Present Regulations of the Food and Drugs Act.*

The Committee completed its study of the Regulations and decided how far it should go in proposing alterations in the requirements of the same. It was the unanimous opinion of its members that no general changes should be contemplated at this time, but that provision for a further orderly review of the whole problem should be made, on the basis of a continuing study, after this report has been submitted. Five specific recommendations for changes in the requirements of the Regulations were prepared, at a meeting held apart from the Food and Drug Directorate. The chairman subsequently discussed them with the Director, and other officials of the Department, on November 23rd, 1962, and it was after this discussion that the documents in Appendix No. 6 were prepared.

Recommendations with Respect to Changes in the Regulations, at the Present Time.

1. *C.01.301:*

(1) With respect to this Section, the Committee is of the opinion that the ultimate effectiveness and safety of a "new" drug can be determined only by its use by a body of practitioners* over a sufficiently long period of time to enable qualified persons to make such an evaluation from accumulated data.

Therefore, the Committee recommends to the Minister that after a Notice of Compliance has been issued, greater controls than at present be exercised with respect to the drug, and for such time as deemed necessary by the persons qualified to evaluate these matters, unless, in the opinion of the Minister, such controls are unnecessary.

(2) In the opinion of the Committee these controls should include:

(a) dispensing by prescription only,

(b) indications that the drug is newly introduced, or a new formulation, on labels and promotional material,

(c) manufacturer to report toxic reactions promptly,

(d) responsibility of the practitioner to report adverse reactions either directly or through appropriate local organizations,

(e) notification of appropriate national bodies of the issuance of Notices of Compliance.

* Persons legally qualified to use drugs in the treatment of man or animals.

2. *C.01.302:*

With respect to this Section the Committee recommends to the Minister that there should be added: "Substantial evidence of clinical effectiveness for the purpose intended".

3. *C.01.307:*

With respect to this Section the Committee recommends to the Minister that:

(1) Subsection (a) be amended to read:
"the Minister is first informed of the objectives of the trial, the identifying name or mark by which the drug can be recognized, and the chemical structure, if known, or other specific identification of the composition of the drug".

(2) Subsection (d) be amended to read:
"the manufacturer keeps accurate records of such distribution and of the results of such investigation and makes those records available for inspection on the request of the Director,
and
the manufacturer informs the Minister prior to distribution of the name(s) of the Qualified Investigator(s), and the institution(s) in which the investigation is to be carried out;
and
all data with respect to serious toxicity are reported immediately, both to the Minister and to the manufacturer.

Drugs included under this Section shall be known as "Investigational Drugs".

4. The Committee recommends to the Minister that the Minister be empowered to order the cessation of any clinical trial, or limit the trials to certain qualified investigators, in his discretion.

5. The Committee recommends to the Minister that the Minister be empowered to suspend or withdraw a Notice of Compliance, in which case the drug shall revert to the status of an Investigational Drug.

9. *Need for Continuing Study of the Overall Problem of Food and Drugs.*

While the terms of reference of this Committee were most specific with respect to the present procedures of the Department for dealing with new drugs, and the requirements of the Regulations, there was also contained in these terms the phrases "and any other matters that, in the opinion of the Committee, are relative to the issue". In the course of this investigation the Committee has received the greatest cooperation and the most earnest consideration of its requests for information and recommendations from the numerous and varied bodies that it consulted, visited, or with whom it could only correspond. The attached appendices contain a wealth of information that relates, in some instances at least, to matters that are much broader than those concerning "new" drugs. However, whether related to "new" drugs or not, these matters (such as drug dosages in children, carcinogenesis as it may be related to drugs, teratogenesis, blood dyscrasias, poison control, hazardous drugs, allergies as related to drugs, etc.) are of vital concern to the health of the people of Canada, and hence to this department.

It has become abundantly clear to the members of this Committee as they have proceeded with this investigation that:

(1) There is a need for a careful and painstaking review of all drugs, not merely "new" drugs, as suggested in the preceding paragraph, and continuing surveillance.

(2) The roles of insecticides, pesticides, and other chemicals not properly designated as "drugs", in the causation of ill health should be delineated, and controlled.

(3) the role of drugs used in veterinary medicine should be a subject of continuing study and from the standpoint of their possible effect(s) on human health.

(4) The matters covered in the preceding three paragraphs should be the subject of continuing intensive study by the department, through the Food and Drug Directorate, and a special committee empowered to meet with the necessary additional specialists or experts in the particular field under scrutiny.

(5) Such a committee as envisaged in paragraph (4) should be composed of a small number of expert and dedicated individuals with overlapping appointments of short term (or relatively short term) duration, who have (or will make) the time available to carry out the continuing studies indicated above, and such others as the committee may deem advisable.

There is already in existence an Advisory Committee to the Food and Drug Directorate, known as the Canadian Drug Advisory Committee (C.D.A.C.), which was established by Order-in-Council (P.C. 1958-830) on the 12th day of June 1958. (Appendix No. 8). This is a relatively large committee consisting of some 14 members at the present time, three of whom are permanent, and others who are appointed by the Minister for periods of three years.

This Committee (C.D.A.C.) has the power to appoint or designate sub-committees, to consult with such persons as may be deemed necessary or advisable, in regard to matters respecting drugs, including Regulations made or proposed to be made for drugs under authority of the Food and Drugs Act.

RECOMMENDATION:

The Special Royal College Committee, therefore, recommends to the Minister that a *working* STANDING DRUG COMMITTEE consisting of a small number of experts, predominantly medical, with overlapping appointments of short term duration, be appointed, either from the Canadian Drug Advisory Committee, or from other sources, to consult with such persons as may be deemed necessary or advisable, in regard to matters respecting drugs, including Regulations made or proposed to be made for drugs under authority of the Food and Drugs Act, and such other matters as the STANDING DRUG COMMITTEE may deem to be in the best interests of the health of the people of Canada.

10. *Consideration of the Division of the Food and Drug Directorate into Food and Drug Sections.*

Inasmuch as this question has been raised, and referred to, in multiple submissions contained in the appendices to this report, the Committee (Royal College) is of the opinion that this matter should receive the earnest consideration of the STANDING DRUG COMMITTEE, if and when appointed, and that any such move, if contemplated, should avoid overlapping of costly administrative, inspection, and laboratory services, and should have the delineation of the functions of the respective sections determined on the basis of the advice of competent professional and technical authorities.

11. *Further Comments on Matters Contained in the Appendices Attached to this Report.*

As mentioned in Section 9, above, many of the appendices to this report contain detailed observations and recommendations with respect not only to "new" drugs but also to the overall problems of the control of the importation, manufacture, and marketing, of drugs in Canada. There also is a need for a careful consideration of the roles that certain substances, not properly designated as drugs, occupy or might occupy, with respect to the health of the people of Canada.

These matters in the opinion of the Committee, should be the subject of a careful and detailed review by the STANDING DRUG COMMITTEE, if and when appointed by the Minister, as recommended previously, and, which, after consultation with the appropriate bodies, or other experts, should consider possible further revisions or additions to the Regulations. Particular attention is drawn to the recommendations and comments contained in Appendix No. 48.

12. *Summary of Recommendations.*

(1) *Recommendation with Respect to Expansion of the Food and Drug Directorate.*

The Committee recommends to the Minister that immediate steps be taken to increase the personnel of the Food and Drug Directorate by the addition of properly qualified persons. The Director has stated the following requirements and the Committee concurs with the recommendation.

I—*Medical Section.*

(a) Two physicians.
(b) Two veterinary physicians.
(c) One chemist.
(d) One technician.
(e) One stenographer.
(f) Four clerk-typists.

II—*Laboratory Division.*

(a) Pharmacologists—5 man years = 15 persons.
(b) Pharmacists—3 man years = 9 persons.
(c) Bacteriologists—1 man year = 3 persons.

The Committee realizes that it may be difficult to recruit the above personnel in under three years.

The Committee further recommends to the Minister that the remuneration for the personnel so added to the Food and Drug Directorate establishment be commensurate with the qualifications required, and that such additional facilities be provided as, in the opinion of the Director, are necessary for the proper functioning of these additional personnel.

(2) *Recommendations with respect to changes in the Regulations, at the present time.*

1. *C.01.301:*

(1) With respect to this Section, the Committee is of the opinion that the ultimate effectiveness and safety of a "new" drug can be determined only by its use by a body of practitioners* over a sufficiently long period of time to enable qualified persons to make such an evaluation from accumulated data.

* Persons legally qualified to use drugs in the treatment of man or animals.

Therefore, the Committee recommends to the Minister that after a Notice of Compliance has been issued, greater controls than at present be exercised with respect to the drug, and for such time as deemed necessary by the persons qualified to evaluate these matters, unless, in the opinion of the Minister, such controls are unnecessary.

(2) In the opinion of the Committee these controls should include:

(*a*) dispensing by prescription only.

(*b*) indications that the drug is newly introduced, or a new formulation, on labels and promotional material.

(*c*) manufacturer to report toxic reactions promptly.

(*d*) responsibility of the practitioner to report adverse reactions either directly or through appropriate local organizations.

(*e*) notification of appropriate national bodies of the issuance of Notices of Compliance.

2. *C.01.302:*

With respect to this Section the Committee recommends to the Minister that there should be added: "Substantial evidence of clinical effectiveness for the purpose intended".

3. *C.01.307:*

With respect to this Section the Committee recommends to the Minister that

(1) Subsection (*a*) be amended to read:
"the Minister is first informed of the objectives of the trial, the identifying name or mark by which the drug can be recognized, and the chemical structure, if known, or other specific identification of the composition of the drug";

(2) Subsection (*d*) be amended to read:
"the manufacturer keeps accurate records of such distribution and of the results of such investigation and makes those records available for inspection on the request of the Director;
and
the manufacturer informs the Minister prior to distribution of the name(s) of the Qualified Investigator(s), and the institution(s) in which the investigation is to be carried out;
and
all data with respect to serious toxicity are reported immediately, both to the Minister and to the manufacturer".

Drugs included under this Section shall be known as "Investigational Drugs".

(4) The Committee recommends to the Minister that the Minister be empowered to order the cessation of any clinical trial, or limit the trials to certain qualified investigators, in his discretion.

(5) The Committee recommends to the Minister that the Minister be empowered to suspend or withdraw a Notice of Compliance, in which case the drug shall revert to the status of an Investigational Drug.

(3) *Recommendation with respect to the establishment of a Standing Drug Committee.*

This Committee recommends to the Minister that a *working* STANDING DRUG COMMITTEE, consisting of a small number of experts, predominantly medical, with overlapping appointments of short term duration, be appointed

either from the Canadian Drug Advisory Committee, or from other sources, to consult with such persons as may be deemed necessary or advisable, in regard to matters respecting drugs, including Regulations made or proposed to be made for drugs under authority of the Food and Drugs Act, and such other matters as the STANDING COMMITTEE may deem to be in the interests of the health of the people of Canada.

13. *Conclusion.*

In conclusion, the Committee, is indebted to the Minister, the Deputy Minister, and the Director of the Food and Drug Directorate and the senior members of his staff, and to all bodies and individuals who have attended the interviews, and made submissions to the Committee, during this investigation, for their tremendous interest, long hours of work, unfailing courtesy, and friendly co-operation.

The Committee further wishes to emphasize that the Directorate has operated under the most difficult conditions, particularly in the last few years, and it is astonishing that it has been able to establish an enviable record of accomplishment. This record of conscientious and fair-minded dealing with manufacturers, pharmacists, and practitioners, is attributable, in large part, to the Director. Beset on the one hand by manufacturers requesting speedy action, and on the other by a duty to protect the public from hazards of which they (and he) might be unaware, his course of action deserves the highest commendation. The Committee feels that the Director has performed his duties with the care, wisdom, and high motivation the public expects from its senior servants.

All of which is respectfully submitted.

(signed) F. S. BRIEN
F.S. Brien, B.A., M.B., F.R.C.P. (Lond), F.R.C.P. (Canada), F.A.C.P.
Chairman.

(signed) R. R. DUFRESNE
R. R. Dufresne, B.A., M.D., F.R.C.P. (Canada),
Member.

(signed) E. A. SELLERS
E. A. Sellers, M.D., Ph.D.,
Member.

INDEX OF APPENDICES

20. Correspondence to and from Dr. J. Wendell Macleod, Executive Secretary, The Association of Canadian Medical Colleges.

21. Information on New Drugs, prepared by J. G. Aldous, Professor of Pharmacology, Dalhousie University, Halifax, N.S., and approved by the Faculty of Medicine for Special Committee of the Association of Canadian Medical Colleges (should read "Special Committee on New Drugs of the Royal College of Physicians and Surgeons of Canada").

22. Comment re Special Committee on New Drugs, by A. Fidler, Professor of Medicine, University of Ottawa, Ottawa, Ontario.

23. Letter and Reprint from Dr. E. M. Boyd, Head, Department of Pharmacology, Queen's University, Kingston, Ontario.

24. Communication from Dr. K. J. R. Wightman, Professor of Medicine, University of Toronto, "Observations Regarding Legislation on New Drugs".

25. Communications from the University of Western Ontario—by Dean O. H. Warwick, and Dr. R. A. H. Kinch, Professor of Obstetrics and Gynaecology.

26. Communications from the University of Saskatchewan, by Dr. A. A. Bailey, Professor of Medicine, and Dr. G. M. Wyant, Professor of Anaesthesia.

27. Report of Faculty of Medicine, University of Alberta to the Special Committee on New Drugs of the Association of Canadian Medical Colleges (should read "of the Royal College of Physicians and Surgeons of Canada").

28. Memorandum to the Special Committee on New Drugs, from the Dean's Committee on Therapeutics, Faculty of Medicine, University of British Columbia.

29. Letter from Dr. John C. Laidlaw, President, Canadian Society for Clinical Investigation.

30. Communication from the Canadian Medical Association—containing extract from its submission to the Royal Commission on Health Services.

31. Submission from Dr. D. L. McNeil, Chairman, Committee on Pharmacy, Canadian Medical Association.

32. Letter from Dr. K. J. R. Wightman, relative to Drug Testing.

33. Correspondence from the Canadian Dental Association—L'Association Dentaire Canadienne.

34. Memorandum of the Canadian Pharmaceutical Association Inc.

35. Suggestions for the Handling of Investigational Drugs in Hospitals, by the Canadian Society of Hospital Pharmacists.

36. Letter from Verdun Protestant Hospital regarding The Early Clinical Drug Evaluation Unit of the Verdun Protestant Hospital.

37. Mémoire présenté à la Commission Royale d'Enquête sur les Services de Santé par L'Association des Fabricants du Québec de Produits Pharmaceutiques.

38. Letter to Mr. André Désautels, Registrar, College of Pharmacists of the Province of Quebec.

39. Letter from Mr. R. E. Curran, Q.C., Office of the Legal Adviser, Department of National Health and Welfare, Ottawa.

40. Correspondence with The Canadian Medical Protective Association, Ottawa.

41. Initial Correspondence from Royal College of Physicians and Surgeons of Canada setting up the Special Committee on New Drugs.

42. Correspondence to and from Dr. C. A. Morrell.

43. Data re Staff of Food and Drug Directorate—Personnel Record Sheets.

44. Letter from the Deputy Minister of National Health relative to Bill C-3, together with a copy of Bill C-3.

45. Brief to the Royal Commission on Health Services from the Medical Section of the Canadian Pharmaceutical Manufacturers Association.

46. Letter to Independent Drug Companies and List of those to whom it was sent.

47. Comments of American Medical Association on Proposal to Amend Regulations Pertaining to New Drugs for Investigational Use, by F. J. L. Blasingame, M.D., Chicago, in the J.A.M.A. of December 1, 1962.

48. Important Comments and Recommendations contained in Submissions made to the Committee.

OFFICIAL REPORT OF PROCEEDINGS AND EVIDENCE

This edition of the Minutes of Proceedings and Evidence contains the text of Evidence in the language in which it was given, and a translation in English of the French texts printed in the Evidence.